Allergy Abstracts

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Allergy Abstracts

Announcement

ALLERGY ABSTRACTS has been published since 1936 by members of the Allergy Division of the Jewish Hospital of Brooklyn. The Editorial Board is comprised of former residents of this department who contribute their services.

ALLERGY ABSTRACTS selects and abstracts those articles in the literature which may be of clinical or theoretical interest to workers in the field of allergy. Each abstract represents a summary of the author's findings and views, and its inclusion in ALLERGY ABSTRACTS does not imply approval of its contents by the editor.

Because of the increasing number of articles dealing with new drugs which are of interest in the field of allergy, a new section on Pharmacology and Physiology has been added to ALLERGY ABSTRACTS, starting with this issue.

—*The Editors.*

Asthma and Hay Fever

Aerosol Therapy of Respiratory Diseases. A Report of Fifty Cases. Bryson, V., and Grace, E. J.: New England J. Med. **237**: 683, 1947.

Aerosol therapy is considered a form of topical treatment. The blood levels obtained with aerosol therapy are more of academic interest than of practical importance. The mechanical equipment necessary for effective aerosol therapy should be simple. Aerosols produced with nebulizers which are clinically effective for treating pulmonary disease should have a particle diameter of 1 or 2 microns. Thirty-four subjects were treated with aerosols of the cationic detergent Zephiran (alkyl dimethyl benzyl ammonium chlorides in aqueous solution) with penicillin. The administration of antibiotics in detergent solutions provides the physical advantages associated with reduced surface tension, the antibacterial advantages contingent on synergism, and the reduced likelihood of drug-fast infection. In preparation for aerosol therapy 0.5 c.c. of a 0.25 per cent solution of neosynephrine is inhaled by the patient. This is followed by deep inhalations of 100,000 units of penicillin dissolved in 3 c.c. of Zephiran in a 1:1,000 aqueous solution every eight hours for ten days. Clinical experience has shown that antibiotic aerosol therapy is a valuable supplement to parenteral penicillin treatment of respiratory disease, including intrinsic infectious asthma, bronchitis, bronchiectasis, and sinusitis. In four cases, urticaria and pruritus followed the administration of penicillin by inhalation. H.

Management of the Asthmatic Attack in Childhood. Ratner, B.: Med. Clin. North America, May, 1947, p. 537.

The treatment of the asthmatic attack in childhood is outlined, and the commonly used drugs are discussed. Adrenalin, two or three minims subcutaneously, is regarded as the drug of choice. Adrenalin in oil and by inhalation are not recommended, the latter because of the tendency to its excessive use. Ephedrine and aminophylline are useful. Histamine, histaminase, and the antihistaminic drugs are of no value, and opiates are con-

traindicated. The author divides asthma into two groups. Symptoms in the first group are due to bronchiolar spasm, and the antigen reaches the bronchioles via the blood stream, as in food sensitive cases. These patients are usually relieved by adrenalin. In the second group, symptoms are due to edema and bronchial plugging caused by inhalants which come directly in contact with the lining of the bronchioles. This group is usually not relieved by repeated doses of adrenalin, but is relieved by syrup of ipecac. Ipecac causes peristaltic waves in the bronchial tree similar to reverse peristalsis in the digestive tract, described as "tracheal vomiting," which releases the obstruction in the bronchial tree by evacuating its contents. It is emphasized that common errors in the treatment of asthma are overmedication and a poor choice of drugs. J. SHERMAN.

Aminophylline With a Barbiturate as a Rectal Suppository in the Treatment of Asthma. Franklin, H. L.: New York State J. Med. **47**: 1242, 1947.

Rectal suppositories containing 0.5 Gm. of aminophylline, 0.1 Gm. of sodium pentobarbital and 0.06 Gm. of benzocaine were administered to sixty-five adult asthmatics. Suppositories of half this strength were prescribed for fifteen asthmatic children. Sixty-nine per cent of adults and 94 per cent of children obtained moderate to marked relief. Thirty-one per cent of cases did not respond to aminophylline at all. Twenty per cent of the adults who used the suppositories continuously over long periods of time developed a tolerance to the drug. Ten per cent of the adult patients experienced side effects such as weakness, nausea, diarrhea, and rectal irritation. Suppositories were particularly effective in epinephrine-fast cases. C.

Evaluation of Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl) in Bronchial Asthma. Fuchs, A. M., Schulman, P. M., and McGadock, T. H.: Am. J. Med. **3**: 309, 1947.

Thirty adults, ranging in age from 20 to 80 years, who had previously received the usual forms of antiasthmatic remedies without success, were given benadryl in an effort to determine the value of this drug in the treatment of bronchial asthma. Eleven in the series were classified as intrinsic asthma and the remaining nineteen as the mixed type. There were no cases of pure allergic (skin sensitive) asthma in the group. All the patients were at first given 50 mg. of benadryl three times daily. If no relief was noted after a trial period of two weeks, the dose was gradually increased to as high as 400 mg. per day. The usual subcutaneous injections of house dust and vaccine were continued throughout the study but all other medications were stopped. The patients were observed over a period of six months. When improvement was reported over a period of four weeks, a placebo was substituted for two weeks. When benadryl was ineffective by itself, it was tried in combination with other medications. Five patients treated with benadryl obtained true symptomatic relief. None of these patients had any evidence of active organic disease of the heart or lungs. The withdrawal of the benadryl was followed by a recurrence of symptoms. Two other patients reported symptomatic relief but experienced similar results with the placebo. All of the twenty-three cases who failed to obtain relief with benadryl showed organic changes in the heart or lungs or active sinus infection. When the drug was used in conjunction with other antiasthmatic agents such as ephedrine, iodides, or aminophylline, there seemed to be a synergic response. Side reactions occurred in 93 per cent of the cases with drowsiness being present in all twenty-eight cases who had reactions. F.

Comparative Action of Acetyl-Beta-Methyl Choline and Histamine on the Respiratory Tract in Normals, Patients With Hay Fever, And Subjects With Bronchial Asthma. Curry, J. J.: J. Clin. Investigation **26**: 430, 1947.

Vital capacity determinations were carried out on ten normal individuals, on eleven persons with hay fever, and twenty-seven with asthma. Histamine and mecholyl were administered intravenously or intramuscularly to all three groups with the following results: both mecholyl and histamine in the dose chosen for testing caused either a slight reduction or increase in the vital capacity of normal individuals. Both of these drugs lowered vital capacity in hay fever patients tested during the pollen season, mecholyl being more active in this respect. While both drugs lowered vital capacity in asthmatics, mecholyl did so more consistently than histamine. The effects were greater when the asthma was active, and were proportional to the dose of the drugs. Prostigmine methyl sulfate markedly enhanced the effect of mecholyl but did not alter the response to histamine. Benadryl counteracted histamine-induced reduction in vital capacity but, in one patient, did not affect the response to mecholyl, indicating that mecholyl does not act through the release of histamine. Subjects were unable to distinguish between mecholyl and histamine except that the effect of mecholyl lasted longer (ten to thirty minutes). Extrapulmonary reactions to mecholyl were essentially the same in asthmatic and nonasthmatic persons. Inhalation of a nebulized 1:40,000 solution of mecholyl sharply reduced vital capacity in asthmatics. This effect in one case was counteracted better by epinephrine than by atropine. It is suggested that the tracheobronchial tree may be more reactive to mecholyl administered by nebulization than by the intravenous route. K.

Pyribenzamine (N-Pyridyl, N-Benzyl, Dimethyl-Ethylenediamine-hydrochloride) in the Treatment of Allergy. Henderson, A. T., and Rose, B.: Canad. Med. Assn. J. **57**: 136, 1947.

Pyribenzamine in an average daily dose of 200 mg. was administered to 138 patients with various allergic complaints. The most favorable results were obtained in a group of sixty-one hay fever victims, forty-seven of whom were benefited. Three of fifteen chronic asthmatics were improved, but in three other patients the drug produced exacerbations of the attacks. Of five patients having migraine, one showed symptomatic improvement. Wheal reactions to scratch tests with ragweed pollen were diminished by 50 mg. of pyribenzamine given an hour prior to testing. Side reactions, consisting of sleepiness, nervousness, nausea, dry mouth, dizziness, insomnia, headache, and vomiting were encountered. In only two instances was it necessary to discontinue the medication, since these reactions usually disappeared after two or three days of therapy. K.

Eosinophilia and Tuberculosis. Kurkijarvi, M.: Nord. Med. **4**: 3717, 1939.

In 200 cases of pulmonary tuberculosis, the author found that the blood eosinophilia was slightly in excess of the upper limit of normal. Sputum eosinophilia of a slight degree was also frequently found in these patients. Since bronchial asthma and pulmonary tuberculosis may coexist, the presence of a blood and sputum eosinophilia in a patient raises the question of the differential diagnosis of these two diseases. The literature on the fluctuations of blood eosinophilia in the various stages of tuberculosis is reviewed. H.

Dermatology

Cutaneous Reactions to Penicillin. Templeton, H. J., Lunsford, C. J., and Allington, H. V.: Arch. Dermat. and Syph. **56**: 325, 1947.

Thirteen cases of contact dermatitis from penicillin were studied. Among these, six patients had used penicillin ointment and in the remainder, the lesions followed the use of penicillin solution in wet dressings. Two cases of conjunctivitis and dermatitis of the eyelids followed the use of penicillin eye drops. Toxic macular or scarlatiniform eruptions following the parenteral administration of penicillin were common. Urticaria, the most common skin reaction, occurred seven to nine days following parenteral administration of the drug. In three patients, the urticaria was associated with signs and symptoms resembling serum sickness. In one there were macules, papules, and painful nodules of the erythema multiforme-erythema nodosa type. Another showed typical lesions of erythema multiforme. Three patients with old dermatophytosis developed a "phytid" reaction within four hours after the parenteral administration of penicillin. Combined dermal and epidermal sensitization was seen in a patient whose healed contact dermatitis, caused by penicillin, recurred within twelve hours after an intramuscular injection of the drug. This was followed by a generalized urticaria.

In passive transfer experiments, cutaneous sites, injected with the sera of five urticarial patients failed to react when penicillin was administered to the subjects parenterally or was applied as a patch test. However, when similar sites were tested by scratching penicillin solution into the area, one- or two-plus reactions were obtained. This was regarded as evidence of circulating antibodies. From these observations and from a comprehensive review of the literature, it is suggested that patients with exudative dermatoses are poor risks for penicillin therapy. E. WALZER.

Dermatitis From Glass Fabrics. Schwarts, L.: Arch. Dermat. & Syph. **55**: 258, 1947.

Attention is called to outbreaks of dermatitis resulting from the use of glass fabrics (fiberglass) as linings in women's suits, babies' coats, or for binding seams in women's dresses. A warning is issued against the use of fiberglass in clothing. C.

Lipstick, a Cause of Cheilitis. Putkonen, T.: Acta Derm-venereol. **26**: 515, 1946.

Positive patch tests were obtained in five of six cases of lipstick dermatitis. In each case the specific factor was found to be the coloring matter. Fat-soluble pigments were the worst offenders. Of the five patients observed, two were also sensitive to eyebrow pencil and one to an elastic headband. C.

Miscellaneous Allergies

Clinical Evaluation of Bovine Serum Albumin as a Blood Substitute. State, D., Romero, F. T., Castellanos, M. M., and Wangensteen, O. W.: Surgery **22**: 424, 1947.

Reactions were observed following the intravenous use of bovine serum fractions as a blood substitute in human beings. Using highly purified bovine serum albumin, 469 injections in 410 patients resulted in immediate reactions in 2.9 per cent and delayed reactions in 9.2 per cent of cases. This was a marked

improvement over the results of previous workers who had reported a 50 per cent incidence of immediate reactions and a 60 per cent incidence of delayed reactions with unpurified bovine plasma and serum. Immediate reactions consisted of either chills and fever or were characterized by dyspnea, cyanosis, and a fall in blood pressure. The delayed reactions occurred twelve to twenty-four hours after the injection and consisted of urticaria, erythema, myalgia, arthralgia, and fever. In severe cases, there were petechiae and ecchymosis. The incidence of reactions was no greater in patients who received multiple injections than in those receiving one injection. Delayed reactions occurred frequently in the absence of a positive skin test and despite a negative history of allergy. Other patients with a positive skin test or history of allergy did not develop reactions. Despeciation of the bovine serum albumin did not eliminate reactions. Intravenous procaine was effective in the treatment of the delayed reactions. Although periarteritis nodosa and pancarditis have been observed in rabbits sensitized to bovine serum albumin, no evidence of periarteritis nodosa or pancarditis was found in patients in this series who came to autopsy. Two of these had reactions, but died of other causes. J. SHERMAN.

Sulfadiazine Sensitivity With Demonstrable Skin-Sensitizing Antibody in the Serum. Sherman, W. B., and Cooke, R. A.: Am. J. Med. **2**: 588, 1947.

The serum of a 24-year-old female who had experienced a severe reaction to sulfadiazine was shown to contain thermolabile antibodies to the drug. A patch test made with 10 per cent sulfadiazine was positive but a similar test with dry powdered drug was negative. Passive transfer tests were positive with sodium sulfadiazine, sodium sulfapyridine and sodium sulfathiazole, but negative with sulfanilamide. Ingestion of sulfadiazine resulted in the lighting up of sensitized sites in forty to ninety minutes. Attempts at in vitro neutralization of the antibody were unsuccessful. Skin sites prepared with a mixture of antibody-bearing serum and sulfadiazine when tested intracutaneously after a forty-eight hour interval reacted to sulfadiazine. Precipitins could not be demonstrated in the serum nor could passive local or general sensitivity be produced with it in guinea pigs. F.

Treatment of Allergy to Insulin With Diphenhydramine Hydrochloride. Report of Two Cases. Leavitt, M.D., and Gastineau, C.: Arch. Int. Med. **80**: 271, 1947.

Diphenhydramine hydrochloride (benadryl) was employed in the treatment of local and generalized reactions in two insulin-sensitive diabetic patients. The intracutaneous injection of 0.2 ml. insulin in dilutions of 1:10 to 1:5,000 produced flares varying from 14.5 cm. to 7.2 cm. in one patient and generalized urticaria in the other. The oral administration of 100 mg. benadryl thirty minutes prior to skin testing reduced the size of the flares from 5 to 86 per cent and the addition of benadryl in 1:1,000 solution directly to the insulin reduced the size of the flares from 75 to 100 per cent. In Prausnitz-Küstner studies, the flare-size was reduced as much as 89 per cent by the addition of 1:1,000 solution benadryl to the insulin. It is suggested that benadryl solution 1:1,000 be employed in the treatment of localized allergic reactions to insulin and other injected substances. E. H. WALZER.

A Clinical Test for Migraine. Schnitker, M., and Schnitker, M.: J. A. M. A. **135**: 89, 1947.

A test to establish the diagnosis of migraine may be performed by administering, sublingually, $\frac{1}{50}$ grain of nitroglycerin to the resting patient. After two

minutes, the pulse rises, the blood pressure usually drops and the patient begins to experience symptoms which are of the same nature as those which constitute the original complaint. The patient can be relieved of these induced migrainous symptoms by compressing the carotid artery or, if that fails, by having the patient breathe 100 per cent oxygen for five minutes or by administering from 0.5 to 1.0 mg. of ergotamine tartrate, intravenously. Patients with a positive reaction to nitroglycerin have been successfully treated for their migraine by the administration of calcium lactate twice daily, the elimination of allergenic offenders and the use of ergotamine tartrate. F.

Successful Desensitization in Penicillin Sensitivity. Peck, S., Siegal, S., and Bergamini, R.: J. A. M. A. **134**: 1546.

Reactions to penicillin may fall into the following four classes: (1) drug or serum-sickness-like reactions or toxic erythemas and severe local reactions following the use of penicillin in beeswax and peanut oil. (2) Contact dermatitis. (3) Erythematovesicular eruptions often beginning and frequently limited to the sites of previous fungous infections on the hands, feet, and groin. (4) Febrile reactions following aerosol inhalation or bronchial instillation of penicillin. Immediate reactions to penicillin skin tests were not observed, but a delayed positive test of the 48-hour type was seen and is believed to be of clinical significance.

A case report of a 63-year-old male who had previously developed a severe generalized erythematovesicular eruption following the administration of penicillin is presented. The patient gave a positive 48-hour test to noncrystalline commercial penicillin. Following a laryngectomy, it became imperative to administer penicillin. An attempt was therefore made to desensitize the patient to penicillin. Subcutaneous injections in gradually ascending doses were given three times a week starting with 400 units of noncrystalline penicillin. Each subsequent dose was doubled so that the sixth dose was 12,800 units. Thereafter the increases were smaller. At the time the dose had reached 20,000 units, a skin test with penicillin gave only a pinhead-sized papule at the 48-hour reading. A trichophytin test (1-30) done simultaneously with the penicillin test was strongly positive. Several days later, intramuscular doses were started which were increased in amount and frequency until doses of 30,000 units were given every three hours. At this time, a cutaneous reaction appeared in the groin and the gluteal regions. Therapy was stopped for twenty-four hours, after which time it was resumed on a reduced schedule and gradually brought back to maximum. The eruption on the groin and buttocks faded gradually. Twenty-seven days after the first negative skin reaction, the patient was retested with crystalline and commercial penicillin with negative reactions to both. F.

Contribution to the Knowledge of Antibody Formation in Infants Following Oral Administration of Chicken Egg White. Uroma, E.: Acta. Soc. Medic. fenn. Duodecim. Ser. A. **3**: 1, 1939.

Forty-eight infants, from one week to seven months of age, were given one raw egg daily for from one- to three-week periods. Complement fixation studies were performed daily and again four weeks after the last dose of egg white. Antibodies for egg white were found in only three cases; inhibition of hemolysis was observed in antigen dilutions ranging from 1:800 to 1:123,600. Two of the three infants developed slight "eczema of the face and neck," which quickly cleared when the feeding of raw egg white was discontinued. H.

Allergic Reactions Following Injection of Vitamin B 1. Kuo, P. T., and Hwang, M. S.: Chinese Med. J. **63**: 7, 1944.

Severe allergic reactions following the intramuscular injection of 10 mg. of thiamine hydrochloride were observed in two patients. In both instances, the reactions occurred after a number of injections had been well tolerated. Marked cutaneous reactions were noted in both cases following intracutaneous testing with the offending thiamine preparation. Other thiamine preparations varied considerably in the degree of positive cutaneous reaction which they elicited. In no instance did any produce such a marked reaction as that obtained with the original thiamine preparation. The authors suggest that the allergic reactions were caused by some unknown antigenic substances rather than by thiamine hydrochloride itself. H.

Anaphylaxis

Neurologic Manifestations in Laboratory Animals Produced by Organ (Adjuvant) Emulsions. Kopeloff, L. M., and Kopeloff, N.: J. Immunol. **57**: 229, 1947.

Neurologic signs were produced in guinea pigs by the single subcutaneous injection of whole organ emulsions or alcoholic extract emulsions of homologous and heterologous brain tissue incorporated in adjuvants. Rabies-infected or uninfected brain, white matter, grey matter, frozen, autoclaved, or boiled brain and rabbit kidney were all effective in producing the reaction. Unfrozen white matter, rabbit liver, neurokeratin, and the adjuvants alone caused no reaction. With rare exception, rats and mice showed no neurologic disturbances following such treatment. The phenomenon was produced in rabbits by subcutaneous injections of whole rat brain or alcoholic extract of sheep brain and egg white incorporated together in adjuvants, given twice a week for a month. Anti-brain antibodies in titers ranging from 1:1,280 to 1:5,120 were produced in rabbits but the titers bore no relation to the neurologic manifestations. No evidence of anti-brain antibodies was obtained in guinea pigs. Skin tests on guinea pigs sensitized with rabbit brain were positive when tested with rabbit brain and rabbit testicle antigen, but not with guinea pig brain antigen. Guinea pigs injected with guinea pig brain emulsions gave negative skin reactions to all types of brain and organ antigens. Guinea pigs treated with neurokeratin emulsion showed positive reactions with rabbit brain and neurokeratin. It seems probable that there is a common antigen in brain, kidney and testicular tissue.

B. Siegel.

Isoallergic Encephalomyelitis and Radiculitis in Guinea Pigs After One Injection of Brain and Mycobacteria in Water-in-Oil Emulson. Freund, J., Stern, E. R., and Pisani, T. M.: J. Immunol. **57**: 179, 1947.

The majority of guinea pigs which had received a single subcutaneous injection of rabbit or guinea pig brain in a water-in-oil emulsion with killed acid-fast bacilli, developed hind leg paralysis in three or four weeks. When all of the adjuvants, or bacilli were omitted from the brain emulsion, or when guinea pig serum, heart or kidney was substituted for brain, the animals remained normal. Mice, injected with rabbit brain plus adjuvants, did not develop paralysis. Several guinea pigs sensitized with rabbit brain plus adjuvants gave positive delayed local reactions, and occasionally systemic reactions, on intracutaneous testing with rabbit brain. This did not occur when guinea pig brain was used as the sensitizer. Histologically, the lesions were confined to the central nervous system and demonstrated primarily hyaline and leucocytic thrombi in the blood vessels, perivascular infiltration with mononuclear cells, and occasionally hemorrhages. These lesions were found in the meninges, parenchyma

of the cerebral hemispheres, and, to a lesser degree, in the spinal cord and anterior spinal roots. Other organs were not affected. It is assumed that the encephalomyelitis produced in guinea pigs with guinea pig brain injections is on the basis of isosensitization. The fact that rabbit brain injections can produce similar lesions in guinea pigs can be explained by the organ-specific nature of some of the antigens of brain tissue. B. SIEGEL.

Effect of Rutin in Anaphylactic and Histamine Shock. Raiman, R. J., Later, E. R., and Necheles, H.: Science **106**: 368, 1947.

The intraperitoneal administration of 2 mg. of Rutin protected horse-serum-sensitized guinea pigs from anaphylactic shock but failed to protect normal guinea pigs from shocking doses of histamine. It was not established whether the protective action of Rutin is due to its effect upon capillary permeability or to unknown factors which prevent the liberation of endogenous histamine. F.

Effect of Antihistaminic Substances on the Edema Produced by Egg White in the Rat. Legar, J., and Masson, G.: Am. J. M. Sc. **214**: 305, 1947.

Powdered egg white injected intraperitoneally into the rat produces an anaphylactoid reaction resembling angioneurotic edema. The antihistaminic drugs, Antisin, Benadryl, and Neoantergan when injected subcutaneously one-half hour before the administration of egg white prevented or diminished the incidence and intensity of this edematous reaction. All animals developed the reaction when the antihistaminic drugs were given twenty-four hours before the administration of the egg white. The ability of an antihistaminic drug to inhibit the edematous reaction in the rat may be an index of its effectiveness against other edematous conditions.

Additional experiments were carried out on rats in an effort to determine whether the liver or kidney played a role in detoxifying or eliminating the antihistaminic drugs. It was shown that partially hepatectomized and completely nephrectomized rats showed no increase in the level of toxicity from Neoantergan, thus demonstrating that the drug is not detoxified in the liver or eliminated by the kidneys but is probably inactivated at its point of action, that is, in all the tissues. F.

Effect of Ergotamine Tartrate on Potassium Changes in Histamine Shock. Tum-Suden, C.: Proc. Soc. Exper. Biol. & Med. **64**: 464, 1947.

The serum potassium changes which occur during histamine shock in normal rats were compared with those occurring in animals receiving ergotamine. Prior to the shocking dose of histamine, the ergotamine was administered for the suppression of adrenergic activity. No significant difference was noted between the ergotamine-treated and normal animals. In demedullated rats, ergotamine reduced the variability in potassium levels. The course of histamine shock was not changed symptomatically in intact or demedullated rats by the administration of ergotamine. E. WALZER.

Miscellaneous

Histological and Serological Sequences in Experimental Hypersensitivity. Hawn, C. V. Z., and Janeway, C. A.: J. Exper. Med. **85**: 571, 1947.

Approximately sixty male rabbits were injected intravenously with large single doses of crystallized bovine serum albumin, highly purified bovine serum gamma globulin, or sterile bovine serum. Antigen and antibody deter-

minations were made weekly on the sera by a precipitin technique. Some animals of each of the three experimental groups were sacrificed weekly for four weeks for pathological examination.

After the injection of serum albumin, lesions, which were confined almost exclusively to the arteries, were maximal at two weeks. Three of five animals had extensive lymphocytic and monocytic infiltration of the intimal and subintimal coats of the larger pulmonary vessels, great vessels of the heart, the valvular endocardium, and the mesenteric arteries. Fibroblasts were proliferative and there were scattered polymorphonuclear leucocytes and eosinophiles in the lesions. One animal had a mild glomerulonephritis. At three weeks lesions were found in a reparative stage and reparation was almost complete at four weeks. Only eight of twenty animals that received the serum albumin showed the above lesions. Antigen disappeared from the circulation at about three weeks.

Bovine serum gamma globulin produced a sequence of lesions strikingly different from those following crystallized bovine serum albumin. One week after the injection of globulin the lesions were maximal. At this time the kidneys were pale and turgid. The glomerular cell nuclei were about twice as numerous as normal and occasional mitotic figures were found. The capillary endothelium was swollen so that the glomeruli were relatively bloodless. There was moderate infiltration with monocytes and a few polymorphonuclear leucocytes were present. Precapillary arterioles and other vessels of the kidney were unchanged. No acute lesions were demonstrable at two, three and four weeks, but glomerular scarring without evidence of a chronic inflammatory process was evident. Systemic arterial lesions in these animals were rare and, in general, limited to the great vessels of the heart and lungs, and to the heart. Several animals had lesions resembling Aschoff bodies. Valvulitis and myocarditis were prominent, and collagenous fibers in the heart were swollen, fragmented, and stained poorly. The arterial lesions resembled those elicited by the albumin and healed without scarring, within four weeks. In this group of animals, changes in the focal accumulations of monocytes and lymphoid cells were found in the joint synovial subserosa in many of the rabbits. Joint changes were not found in albumin-sensitized animals. Nearly every animal showed tissue changes, attributable to hypersensitivity. The bovine globulin disappeared from circulation in from one to two weeks and precipitins appeared promptly thereafter.

Sterile bovine serum was administered to a third group of rabbits and the resultant vascular lesions were essentially the same as observed by other workers with horse serum. They also resembled the lesions obtained with crystalline serum albumin but were more acute.

The lesions described do not occur spontaneously in rabbits. They were carefully differentiated from lesions of spontaneous interstitial myocarditis and from lesions due to Encephalitozoon cuniculi infection. In general, acute lesions appeared when antigen was still in circulation and healing was associated with the disappearance of antigen and appearance of antibody. Surprisingly, the reticulo-endothelial system was spared apparent tissue damage. Since lymphocytes have been found to contain high concentrations of antibody and since antigen may be localized in certain tissues, it is postulated that after the intravenous injection of antigen there is selective localization of the antigen in arterial walls and elsewhere and that antibody may either be carried to these sites by lymphocytes or monocytes or may be elaborated at these sites by fixed tissue cells, with resultant localized damage. K.

Inhibition of Primary Tuberculosis by B C G. A Study in Children, Based on 13,470 Chest Roentgenograms. Neiman, I. S., and Loewinsohn, E.: Am. Rev. Tuberc. **56**: 27, 1947.

A significantly higher incidence of primary tuberculosis was found in a group of 1,414 unvaccinated children than in a group of 1,417 children vaccinated with B C G from four to six days after birth. These children lived in Chicago areas where there was a high tuberculosis rate, but there was no known tuberculosis in their homes. They received repeated physical and x-ray examinations and tuberculin tests at six-month intervals for periods up to seven years. K.

Activity of Histamine in Plasma. Emmelin, N.: Acta Physiol. Scandinav. **Vol. 2** (Suppl. 54), 1945.

Plasma ultrafiltrate was found to contain histamine in approximately the same concentration as that present in a sample extracted chemically. The histamine content of aqueous humor was about the same as that of plasma. Cross circulation experiments in guinea pigs verified the conclusion that the histamine in circulating plasma is present in an active form. The histamine concentration of the plasma in cats can be raised by the slow intravenous injection of histamine without producing a significant depression in the blood pressure. H.

Histamine Excretion Following Excessive Doses of Histidine. Holtz, P., and Credner, K.: Hoppe-Seyler's Ztschr. f. Physiol. Chem. **280**: 1, 1944.

Increased amounts of histamine can be demonstrated in the urine of guinea pigs following the intramuscular injections of large doses of histidine. This indicates that the amine in this instance is not the result of bacterial action but is produced by the intermediary metabolism of histidine through histidine carboxylase. This probably occurs in the kidney. H.

Pharmacology and Physiology

Clinical Uses of Histamine and Histaminase—An Evaluation. Curry, J. J.: Med. Clin. North America, Sept., 1947, page 1261.

Histamine has both diagnostic and therapeutic uses. Histamine has been employed as a test of gastric function. A failure of hydrochloric acid response in the stomach after the subcutaneous injection of 0.25 to 0.50 mg. of histamine base indicates permanent achlorhydria. Histamine is useful as a diagnostic test for pheochromocytoma by inducing attacks of paroxysmal hypertension in such cases. The intravenous injection of 0.01 to 0.04 mg. of histamine base in asthmatic patients induces an "asthmatic-like" attack with a reduction in vital capacity. Such a response might rule out hysteria or malingering where suspected. A positive response, however, is not diagnostic of bronchial asthma, since patients with bronchitis and emphysema may react in a similar manner. The time required for histamine to reach the vessels of the face following its intravenous injection has been used as a measure of circulation velocity, but severe reactions may occur in patients with asthma, bronchitis, and emphysema. The histamine flare following its intradermal injection depends on adequate local arteriolar circulation and intact peripheral nerves. If the nerves are intact, the absence of the flare indicates poor arteriolar circulation. The test is of value in establishing the site for amputation of an extremity. If the circu-

lation is intact, the absence of the flare indicates peripheral nerve degeneration and may be useful in differentiating organic from hysterical anesthesia. In small doses, histamine has been used in the treatment of hay fever and asthma. It is recommended in the treatment of histamine cephalgia, migraine, and Ménière's disease. Its value in the treatment of multiple sclerosis has not been established. Histaminase slowly inactivates histamine in vitro. The early promising reports of its use in treatment of allergic conditions have not been confirmed. J. SHERMAN.

Studies on the Pathogenesis of Rheumatic Fever. I. Experimental Production of Autoantibodies of Heart, Skeletal Muscle, and Connective Tissue. Covelti, P. A.: Arch. Path. **44**: 1, 1947.

Rats were injected with mixtures of killed streptococci and emulsions of rat tissues such as heart, skeletal muscle, and connective tissue. Antibodies were formed which reacted in vitro with extracts of the corresponding tissue injected. Antibodies were not found when the emulsion was injected without streptococci. The tissue components may act as haptens, since the antibodies formed can react with them in the absence of the organisms. J. SHERMAN.

Studies on the Pathogenesis of Rheumatic Fever. II. Cardiac Lesions Produced in Rats by Means of Autoantibodies to Heart and Connective Tissue. Cavelti, P. A.: Arch. Path. **44**: 13, 1947.

Rats were given a series of injections containing mixtures of killed streptococci and emulsions of rat heart or connective tissue. The rats were killed and autopsied from seven to one hundred twenty days later. Changes were most marked in the connective tissue structures of the heart, particularly the valves. These changes resembled those of rheumatic fever in human beings. These findings suggest a possible pathogenesis for rheumatic fever. In the two or three weeks following a streptococcic infection, an antigen may be formed by the reaction between the streptococci or their products and the tissues of the host, probably connective tissue. Specific antibodies are formed, which produce the rheumatic lesions by reacting with the antigen in the tissue.
J. SHERMAN.

A Study of Comparative Antihistamine Activity of Six Compounds. Winter, C. A.: J. Pharmacol. and Exper. Therap. **90**: 224, 1947.

Simultaneous studies were carried out to determine the antihistaminic and toxic properties of Benadryl, Pyribenzamine, Hetramine, Neoantergan, and two compounds designated as "#3015 R. P." and "#3277 R. P." A constant dose of histamine was administered intravenously or by aerosolization to guinea pigs, and the dose of the antihistaminic drug was varied to determine the smallest protective amount. The antihistaminic drugs were injected subcutaneously thirty minutes prior to the exposure to histamine. The contraction heights of strips of guinea pig ileum in baths containing constant amounts (by weight) of antihistaminic drug and histamine were also studied. In all three tests, the decreasing order of antihistaminic potency was: Neoantergan, Pyribenzamine, "3015 R. P.," Benadryl, and Hetramine. The acute toxicity in mice was least for "3277 R. P.," benadryl, and neoantergan, and greatest for hetramine and pyribenzamine, but in all instances the toxic levels were far above the thera peutic dose. Delayed deaths occurred following the administration of "3277 R. P." and benadryl. The therapeutic index was highest for neoantergan. K.

Age and Lung Histamine. Trethewie, E. R.: J. Immunol. **56**: 211, 1947.

The histamine content of the lungs of guinea pigs of varying ages was determined. The foetal lung of the 2.8 cm. guinea pig contained negligible quantities of histamine. Thereafter, definite trends were noted when the histamine content was expressed as γ/g lung or γ/g animal. Expressed in this fashion, the histaminic content of the lungs of animals at term was extremely high (219 γ/g lung). By the fifty-sixth day, the histamine content in γ/g lung had fallen one-quarter of the content at birth. Thereafter, there was a small, gradual increase in the values. Expressed as total-histamine content of the lung, there was little variation between the values at birth and those of the lungs of eight-week animals. In older age groups, the total histamine content of the lungs was greater. The standard deviations for values of animals at term and at eight weeks were small. The standard deviations of lung-histamine values of twenty-week animals was two and one-half times those of the eight-week group. The variations in standard deviations suggest that the histamine content of the lung may be a result of external stimuli. E. WALZER.

Migraine Headache, Treatment of Fifty-One Patients With Dihydroergotamine. Blumenthal, L. S., and Fakler, B.: Med. Ann. District of Columbia **16**: 10, 1947.

Forty-five women and six men experienced a total of 256 various typical migraine headaches during the course of this study. Twenty-two of these patients previously had been given ergotamine tartrate. Ten had discontinued this drug because of its side effects. Dihydroergotamine (D. H. E.), in doses of 1.0 mg., afforded excellent relief to forty-one patients (80 per cent) during 249 attacks. Good relief was obtained in four patients during four attacks and six patients (12 per cent) had little or no relief during thirteen attacks. These results were slightly better than those observed with ergotamine. Toxic effects from Dihydroergotamine were observed in 26 per cent of the patients but did not necessitate discontinuance of the drug. Toxic effects consisted of local burning sensations at the site of injection, pain in the thighs, sensations of burning over the scalp and of the "hair standing on end." Other complaints such as emesis, nausea, fullness of the head, generalized aches, and nervousness were encountered but were believed to be manifestations of the migraine attack which had heretofore been overshadowed by the severe headache. K.

Allergy Abstracts

Asthma and Hay Fever

Chemical Factors in Asthma. Wiswell, J. G., and Rackemann, F. M.: New England J. Med. **257**: 364, 400, 1947.

The authors present an extensive review of the literature on chemical factors in asthma.

The Acid-Base Balance.—The available evidence indicates that potential alkalosis is not a constant factor in allergic patients. The poor pulmonary ventilation in asthma rather causes a retention of excess CO_2 in the blood with a compensatory rise in plasma bicarbonate level and the administration of hydrochloric acid in such patients increases the excess CO_2. If the excess CO_2 cannot be eliminated through the lungs, dyspnea may become increased. The administration of alkali compensates for the excess CO_2 only for a time.

Sodium, Potassium, and Water Balance.—Evidence concerning the roles of these substances in allergy is confusing and conflicting. There is no indication that changes in electrolyte and water balance are specific or that they are a fundamental factor in the symptom complex of asthma. Any marked shift in water balance may aggravate or improve asthma.

Calcium, Phosphorus, and Magnesium.—There does not appear to be any important disturbance in the metabolism of these elements. Any beneficial effects resulting from the administration of these salts probably results from the pharmacologic effects of these compounds on the neuromuscular mechanism.

Blood Sugar.—The writers conclude that there is no relationship between the blood sugar level and asthma.

Cholesterol and Fat Metabolism.—The metabolism of cholesterol is not entirely clear and it is difficult to state whether cholesterol is concerned with allergy. Cholesterol does have a special function in the metabolism of unsaturated fatty acids; however, the role of these acids in allergic states has not as yet been completely clarified.

The Vitamins.—Although deficiencies of vitamin C or niacin probably do not cause asthma, they may aggravate existing asthma. There are as yet no conclusive studies on the relationship of blood chlorides, blood globulin, or nitrogen metabolism and asthma. Such studies would be important in indicating whether asthma, eczema, etc., belong with Selye's "diseases of adaptation." The function of the adrenal cortex in asthma has also not been investigated. H.

Emotions in the Allergic Individuals. Metzger, F. C.: Am. J. Psychiat. **103**: 697, 1947.

Neurotic factors are frequently of considerable importance in atopic patients. Fears and fixed ideas may be precipitating causes of allergic symptoms and emotional complications must be evaluated by the allergist. In many patients relief from an exacerbation of symptoms cannot be explained by the removal of offending allergens. A case is cited in which hay fever was induced by exposure to artificial roses. A psychoneurotic patient, who had given a history of violent hay fever on exposure to goldenrod, was received in the consultation room where a spray of artificial goldenrod had been placed inconspicuously in a corner. The patient was very comfortable until he spied the goldenrod. He then developed a violent attack of hay fever. Physical examination revealed pale and edematous nasal mucous membranes. The attack subsided within five minutes after the patient was shown that the goldenrod was artificial. H.

Peat, Hay Fever, and Pharmacognosy. Wallis, T. E.: Nature **159**: 525, 1947.

The significance of pollen in geology depends on its resistance to decay.

The study of pollen granules in peat layers yield information on the type of vegetation present at different periods. Pollen surveys in Great Britain indicate that clinically the effective pollen season runs from early March until late September. This period can be divided into three phases: (1) tree pollen; (2) grasses; (3) dicotyledonous barks. H.

Dermatology

The Management of Urticaria Due to Penicillin. Pillsbury, D. M., Steiger, H. T., and Gibson, T. E.: J. A. M. A. **133**: 1255, 1947.

Urticaria is the most common type of skin reaction encountered following the parenteral use of sodium penicillin. In the authors' experience, penicillin reactions are more frequently encountered in patients who have had repeated courses of the drug. Some patients who have had an urticarial reaction to penicillin may tolerate further therapy while others may not. Skin tests with penicillin are unreliable as a means of predicting the occurrence of reactions to penicillin on further administration of the compound. Anti-histamine compounds, particularly benadryl, are useful in controlling penicillin urticaria but urticarial reactions may at times be persistent and severe. Fifteen cases of urticaria following the administration of penicillin were observed among a series of 824 individuals under treatment for syphilis. None of the patients had a personal history of allergy. Of the fifteen cases, one developed urticaria after each of his two seven-day courses of penicillin and another developed a morbilliform eruption on the fifth day of her first course of treatment. Seven patients reacted after a second course following an uneventful first course. Five had hives during or after a third course following two uneventful preceding courses. In one case, three uneventful courses preceded the reaction which came after completion of the fourth course of penicillin therapy. It was sometimes possible to continue the use of penicillin in the presence of a reaction by the simultaneous administration of one of the antihistaminics. F.

Urticarial Reaction to Intramuscular Penicillin. A Report of Four Cases. Steingold, L.: Lancet **1**: 468, 1947.

Intracutaneous tests with penicillin X and Y were positive in four patients who had developed urticarial reactions following intramuscular penicillin. Tests with pure penicillin gave negative results. Control subjects tested with penicillin X and Y showed negative reactions. The urticarial reactions were attributed to impurities in the penicillin. In one case, positive cutaneous reactions were still present six weeks later. H.

Aminophylline as an Antipruritic Agent. II. Intramuscular Injection. Epstein, E.: Arch. Dermat. & Syph. **56**: 373, 1947.

Seventeen patients with intractable itching of various types received 0.5 Gm. of aminophylline intramuscularly. Seven experienced dramatic relief within thirty to forty-five minutes. In one patient, relief lasted up to six days but others required daily injections. All patients experienced severe local pain or stiffness and numbness of the leg following injections. Other unpleasant reactions included nausea in three patients and shock in one. It is concluded that local and general reactions limit the general use of this drug as an antipruritic agent. E. WALZER.

Cutaneous Reactions With the Virus of Herpes Simplex. Rose, H. M., and Molloy, E.: J. Immunol. **56**: 287, 1947.

Forty-three persons, ranging in age from 4 to 68 years, were skin tested intracutaneously with 0.1 ml. of herpes simplex antigen prepared from the infected chorioallantoic fluid of chick embryo. Positive reactions occurred in twenty-six patients. They consisted of areas of erythema associated with induration which were maximal in twenty-four hours. In about one-half of the positive reactors, there was an immediate response in the form of whealing and erythema. Two of the positive reactors showed only the immediate type reaction. Thirteen patients showed negative reactions and this group included all of the children. All of the positive reactors and none of the negative reactors showed the presence of neutralizing antibodies for herpes simplex virus in their sera. The four remaining patients had neutralizing antibodies in their sera and all showed immediate positive reactions to control chorioallantoic antigen as well as to the virus antigen. At twenty-four hours, the control antigen sites in three of these were negative and the virus-antigen sites were positive. Only one patient in the entire series gave a history of sensitivity to egg protein. It is concluded that a positive cutaneous reaction to herpes antigen is closely correlated with the presence of neutralizing antibodies in the blood. E. WALZER.

Poisoning Due to Tincture of Rhus Toxicodendron. Lewenburg, H., Jr.: J. A. M. A. **135**: 91, 1947.

A case of poisoning from an overdose of Rhus toxicodendron in an 11-year-old boy is reported. The patient had been taking increasingly large doses of tincture of Rhus toxicodendron at irregular intervals. The last dose taken before the onset of the illness was 57 drops (3.5 c.c.). The patient developed a temperature of 109.2° F., gastritis and signs of central nervous system damage. Treatment was symptomatic and recovery was eventually complete. F.

Urticarial Hypersensitivity to Sunlight. Beal, P. L.: Proc. Soc. Exper. Biol. & Med. **66**: 470, 1947.

Two cases of solar urticaria were studied and their range of sensitivity found to be between 2967 and 3341 Å, with a maximum sensitivity at 3131 Å. This sensitivity could be passively transferred, positive reactions being elicited by exposing the sensitized sites to the active wave lengths. Reactions occurred within thirty minutes and sites remained sensitive for several days. Negative results were obtained with normal control sera. The incidence of positive transfers could be increased by exposing large areas of the patient's body surface to ultraviolet light before withdrawing the blood for passive transfer studies. The serum lost most of its potency by storage at icebox temperature for eight days; was inactivated at 56° C. in one-half hour; and was inactivated by irradiation with ultraviolet light. The sensitizing factor did not dialize through a semipermeable membrane. Some protection against solar urticaria was afforded by an ointment containing 30 per cent G-Salt (sodium salt of 2-naphthol-6,8-disulfonic acid) which absorbed the rays to which the patient was sensitive. Greater protection was afforded by the antihistaminic drugs, which permitted gradually increasing exposures to ultraviolet light for therapeutic purposes. This produced an increased tolerance, limited to the exposed areas which might be attributed to pigmentation and/or thickening of the horny layer of the skin. It is possible that this type of sensitivity may result from the formation of antibodies against a physiological radiation product in the skin. B. SIEGEL.

Group Sensitivity to Local Anesthetics. Confirmation of the Possibility of Its Occurrence and Demonstration That It Does Not Necessarily Always Take Place. Strauss, M. J.: J. Invest. Dermat. **8**: 403, 1947.

Two cases of contact dermatitis caused by local anesthetics are reported. The first patient was a young physician with dermatitis of both hands and fore-

arms for eighteen months. He had been in contact with Pontocaine, cocaine, and procaine for about thirty-three months. Tests by the drop method with twenty-four local anesthetics resulted in a positive reaction only to Pontocaine. Patch tests with the same substances revealed positive reactions to Pontocaine and Apothesine only. The second patient was a young dentist with dermatitis of the fingers following contact with Monocaine, Butyn, Pontocaine and procaine. Patch testing showed positive reactions to procaine, Tutocaine, Monocaine, Larocaine, Pontocaine and Butyn sulfate. These were the substances, in the group tested, which were para-aminobenzoic acid esters with a secondary or tertiary amine in the side chain. This case suggested that sensitization to one or more members of a group of substances could cause sensitization to the whole group. Case one, on the other hand, showed that group sensitivity did not necessarily occur. It is possible that the Pontocaine sensitization may have been so weak that it was unable to cause sensitization to the rest of the group. The incidence of cross-sensitization to all members of a chemically related group may also depend upon individual factors in the patient. B. SIEGEL.

Ragweed Dermatitis (Oral Desensitization). Slater, B. J., Norris, J. L., and Francis, N.: New York State J. Med. **47**: 2322, 1947.

Two cases of dermatitis due to contact with ragweed are reported. Patch tests with ragweed oil were positive. Recurrence of ragweed dermatitis was prevented in one patient by the oral administration of ragweed oleoresin. In the second patient the oleoresin caused repeated flare-ups of the dermatitis. Relief was obtained by removal of the patient to a ragweed-free area. C.

The Local Use of Benadryl Ointment. Perry, D. J.: J. Invest. Dermat. **9**: 95, 1947.

The size of wheals experimentally produced on normal skins and read at ten and fifteen minutes was compared with those produced on sites prepared with 2 per cent Benadryl ointment. Histamine wheals were produced five, fifteen, thirty, forty-five, and sixty minutes after the application of the antihistaminic ointment. Five patients, whose forearms were previously treated with 2 per cent Benadryl ointment, and two, with ointment base alone, showed reactions similar to those of the control. Eight of twenty-two patients with various types of pruritic dermatoses obtained moderate or excellent relief from itching following treatment with 2 per cent Benadryl ointment. When the ointment base alone was used, four of these eight patients obtained similar relief. These results indicate that Benadryl, as used in the above experiments, was not absorbed in sufficient quantities to produce a clinical effect. B. SIEGEL.

Otorhinology and Ophthalmology

Effect of Various Solutions of Penicillin Sodium and Penicillin Calcium on the Respiratory Nasal Mucosa of Rabbits. Fabricant, N. D., Hollender, A. R., and Anderson, H. A.: Arch. Otol. **46**: 36, 1947.

The effect of various solutions of penicillin sodium and penicillin calcium on respiratory nasal mucosa was studied in the rabbit. The nasal mucosa in this animal is more nearly comparable to the human nasal mucosa than that of other laboratory animals. Four drops of solutions of sodium and calcium penicillin containing from 1,000 to 5,000 units per milliliter were instilled three times daily for from thirty to ninety days into the right nasal passages of twenty-one rabbits. The left nasal passages and three untreated animals served as controls. Histologic sections of nasal tissues were made at the end of thirty,

sixty, and ninety days. It was found that the medication produced no ill-effects on the nasal tissues. Penicillin solutions suitable for topical application in the treatment of nasal and sinal infections are compatible with ciliary activity, have a slightly acid pH value approximating that of normal nasal secretions, are isotonic, noninjurious, and nontoxic. C.

Radium Therapy of Recurring Nasal Polyposis. Findlay, J. P.: Med. J. Australia **2**: 71, 1947.

Forty cases of recurring nasal polyposis were treated with radium during the period from 1939 to 1946. The cases were divided into three groups: allergic, infectious, and allergic with secondary infection. Prior to polypectomy a submucous resection of the septum was performed. After polypectomy the ethmoid labyrinth was exposed and all the anterior cells were exenterated. The radium was then inserted. Twenty-eight of these patients were treated with radium element and twelve by radon. A follow-up study revealed only four recurrences, all in patients treated with radium element. There was no evidence of necrosis of cartilage or bone at any time and the nose appeared normal in all cases. H.

Hypersensitivity to Privine. Greenblatt, J.: J. Pediatrics **31**: 355, 1947.

A normal 2-month-old male infant received three drops of 0.05 per cent Privine in each nostril for the treatment of rhinitis. Thirty minutes later, the infant was pale and limp and could not be aroused. The lethargy gradually lessened after three hours, and had completely disappeared after six hours. The infant's brother had had an identical experience at the age of six weeks. A case of a 14-month-old boy who swallowed about 7 c.c. of 0.1 per cent Privine and slept for twelve hours thereafter is also cited. J. SHERMAN.

Sensitivity From Insufflation of the Powdered Sulfonamide Compounds in Acute Infections of the Nose and Throat. Ballenger, H. C.: Arch. Otol. **46**: 52, 1947.

Sulfathiazole, sulfanilamide, and sulfadiazine powders, singly or in combination, were applied by insufflation to the mucous membrane of the upper respiratory tract in 1,500 patients suffering from various acute infections of the nose and throat. Six thousand applications were administered over a three-year period, an average of 2.5 treatments being given for each acute attack. Approximately 0.3 Gm. of powder was used at each treatment. It was found that as a result of treatment the course of the infection was shortened and the number of complications was lessened. Seven individuals (less than 0.5 per cent) among the 1,500 treated gave evidence of sensitivity to the drug, as manifested by dermatitis, hives or hay-fever-like symptoms. C.

The Thyroid Gland and the Nose. Proetz, A. W.: Trans. Am. Laryng. Assoc. in Arch. Otol. **46**: 565, 1947.

Eighty-four patients with chronic vasomotor rhinitis were investigated for thyroid deficiency. Thirty-four were known to have hypothyroidism. In fifty cases in which hypothyroidism was unsuspected the basal metabolic rate varied from minus 10 to minus 40 per cent. The nasal mucosa was often red and turgescent and not always of the pale, boggy type. With thyroid therapy thirty-seven patients were improved, thirty-five showed doubtful results and twelve showed no improvement. There was no relationship between severity of symptoms and basal metabolic rate. C.

Miscellaneous Allergies

Allergy and Blood Transfusion. Schwarts, M.: Nord. Med. **33**: 541, 1947.

Specific antibody can be transferred by transfusion from allergic donors to nonallergic recipients who may develop temporary allergic sensitivity. Allergic

reactions were also observed in allergic patients receiving transfusions of whole blood or dried serum containing specific antigen absorbed from the gastrointestinal tract. Positive reactions could be induced in recipients at cutaneous sites passively sensitized with a high-titer serum by transfusing with blood obtained from donors, who had ingested the specific allergen. Incomplete data suggests that the allergen may be present in the recipient for at least twenty-four hours. It is suggested that allergic individuals should not be employed as donors and that blood for transfusion should be taken after an overnight fasting period. H.

The Quantitative Tuberculin Test: Its Significance in the Diagnosis of Tuberculosis. Woodruff, C. E.: Am. Rev. Tubere. **55**: 488, 1947.

Tuberculin tests with from 1:10,000 to 1:10 dilutions of Old Tuberculin were carried out routinely on patients admitted to a tuberculosis sanatorium. Forty-three patients were found to be anergic. Fifteen of these patients had terminal pulmonary tuberculosis and all of these died within six weeks. There were large numbers of tubercle bacilli in the sputum of these patients except for those having miliary tuberculosis. Of the other anergic patients, one had Pott's disease, nine had tracheobronchial lymphadenitis (three of whom became reactive to the 1:1,000 dilution of O.T. within three months), and twenty-three had miscellaneous nontuberculous illnesses such as atypical pneumonia, sarcoidosis, bronchiectasis, pulmonary fibrosis, and Friedländer's pneumonia. K.

Trichinella Test in Orphanage and in Prison: Comparison With Serologic Tests for Trichinosis and With the Tuberculin Reaction. Harrell, G. T., Horne, S. F., Aikawa, J. K., and Helsabeck, N. J.: J. Clin. Investigation **26**: 64, 1947.

Reports of an unusually high incidence of positive cutaneous reactions to Trichina (Trichinella) antigen in tuberculosis sanatoria and in mental hospitals led to this study of the incidence of such reaction among 285 children in an orphanage and among 241 adult prison inmates. Both Trichina and tuberculin tests were made. Twenty per cent of the orphans and 27.8 per cent of the prisoners showed positive reactions to Trichina. The incidence of reactions appeared to be related to length of institutionalization. Flocculation and precipitin tests carried out on the positive reactors either showed doubtful or negative reactions. No correlation was found between the incidence of Trichina and tuberculin reactions. K.

Immunologic Studies in Insulin Resistance. III. Measurement of an Insulin Antagonist in the Serum of an Insulin-Resistant Patient by the Blood Sugar Curve Method in Mice. Lowell, F. C.: J. Clin. Investigation **26**: 57, 1947.

In a 45-year-old woman with mild diabetes, insulin, in small doses, given after insulin-free periods of five months or more, provoked urticaria, constriction in the chest, and, on one occasion, collapse. Immediately following desensitization with small doses, insulin was effective for three to five days in reducing the patient's blood sugar. However, within eleven to fifteen days from the time desensitization was initiated, the patient became refractory to insulin and a substance appeared in her blood stream which inhibited the effect of insulin on the blood sugar of mice. A technique for rough quantitative measurement of this inhibitory activity is described. The inhibitor was not the glycotropic factor from the anterior pituitary, because when the patient's serum was injected into rats several hours prior to the insulin injection, there was no inhibition of the insulin effect on blood sugar. K.

The Tuberculin Reaction. I. Passive Transfer of Tuberculin Sensitivity With Cells of Tuberculous Guinea Pigs. Kirchheimer, W. F., and Weiser, R. S.: Proc. Soc. Exper. Biol. & Med. **66**: 166, 1947.

Guinea pigs were sensitized by subcutaneous injection of heat-killed *Mycobacterium tuberculosis* in paraffin oil. In some animals an intraperitoneal injection of living B.C.G. vaccine was also given several months later. In others only the single intraperitoneal injection of living B.C.G. was given. Five to nine weeks after sensitization, sterile paraffin oil was injected intraperitoneally into the animals which were most sensitive to tuberculin skin tests. After forty-eight hours, the washed cells of the peritoneal exudate, or of the buffy coat of the minced spleens were injected intraperitoneally into normal guinea pigs. Control guinea pigs received intraperitoneal injections of washed peritoneal exudate cells from animals injected intraperitoneally with paraffin oil without *M. tuberculosis*. Skin tests on the recipient animals with varying dilutions of O.T. were performed forty-eight to seventy-two hours after the cell transfer. Doubtful results were obtained in animals injected with cells from donors sensitized with heat-killed tubercle bacilli alone. The majority of recipients, receiving peritoneal cells from guinea pigs sensitized with heat-killed *M. tuberculosis* and living B.C.G. or with living B.C.G. alone, developed strong typical tuberculin reactions. The recipients of splenic cells usually gave less intense reactions. The transferred cutaneous sensitivity did not last more than five days. Systemic tuberculin reactions starting after three hours were produced in two of the passively sensitized guinea pigs by intraperitoneal injection of O.T. One of these animals died in twenty-four hours. Similarly treated control animals showed no reactions. Thus, passive transfer of tuberculin sensitivity was successfully accomplished. It is suggested that since this type of sensitivity has only been produced with living cells, and only after an incubation period of two or three days, it is possible that the antibody is not preformed but is developed by the cells after their introduction into the recipient.

B. SIEGEL.

Tuberculin Patch Test: A Screening Procedure to Discover Reactors in Children. Neiman, I. S., and Loewinsohn, E.: Am. Rev. Tubere. **55**: 495, 1947.

Tuberculin patch tests, 2,259 in all, were applied to Negro children ranging from infancy to 18 years of age. Of this group, 581 were found to be patch test positive. Fifteen hundred forty-two negative and doubtful reactors were then given Mantoux tests with 1.0 mg. O.T. and an additional 287 tuberculin reactors were discovered, indicating that the patch test is about 67 per cent as efficient as the Mantoux test. One hundred sixty-four children who showed doubtful patch tests were definitely negative on the Mantoux test. Despite the limitations of patch testing for tuberculosis, the ease of administration and increased community cooperation make it a useful survey tool. K.

The Effect of Pyribenzamine on the Tuberculin Reaction in Man. Guy, W. B.: J. Invest. Dermat. **8**: 335, 1947.

Five subjects who showed little variation in their response to three consecutive series of tuberculin tests were selected for the experiment. Each series consisted of intracutaneous injections of 0.1 ml. of Old Tuberculin (Koch) in dilutions of 1:1,000,000, 1:100,000, 1:10,000, and 1:1,000. Test series were performed with freshly prepared Old Tuberculin at intervals of at least one week, by the same observer, using the same needle and syringe for each dilution. The criteria used for reading the reactions were the diameter of the papule and the intensity of the inflammation. With the fourth series of tuberculin tests, 150 mg. of Pyribenzamine was given one hour before, and 650 mg., in divided doses,

within forty-eight hours following each injection. It was found that Pyribenzamine produced no significant effect on the degree of the tuberculin reaction. B. SIEGEL.

Anaphylaxis

Quantitative Aspects of the Inhibition of Anaphylactic Shock in Guinea Pigs. Marcus, S.: Proc. Soc. Exper. Biol. & Med. **66**: 181, 1947.

In a group of guinea pigs, sensitized actively nineteen to twenty-one days previously, the $L.D._{100}$ dose of hen egg white solution, injected intracardially, was found to be 0.1 ml. of a 1:4 dilution. The intraperitoneal injection of 5 to 10 mg. of pyribenzamine or Benadryl, ten to thirty minutes prior to the intracardial injection of approximately 8 $L.D._{100}$ doses of egg white, was sufficient to protect the animals against death from anaphylactic shock. When 10 or more $L.D._{100}$ doses were given to animals prepared with antihistaminic drugs, they died in anaphylactic shock within seven minutes. When six or less $L.D._{100}$ doses of antigen were given, no symptoms were noted. Thus, the antihistaminic drugs exert a quantitative protection against anaphylaxis in actively sensitized guinea pigs, as they also do against histamine shock. The failure of some previous workers to demonstrate active protection against anaphylaxis by these antihistaminic drugs was undoubtedly due to failure to perform their experiments on a quantitative basis. B. SIEGEL.

Effect of Age in Guinea Pig on Local Passive Sensitization and Skin Reactions Toward Histamine. Gottshall, R. Y., and Mitchell, A. B.: Proc. Soc. Exper. Biol. & Med. **66**: 73, 1947.

Young albino guinea pigs from 4 to 10 weeks of age and old animals from 2 to 4 years of age were sensitized intracutaneously, on their backs, with varying dilutions of antiazoovalbumin guinea pig serum and antihorse guinea pig serum. After intervals of from one to four days, varying amounts of the related antigen were injected intra-abdominally. Usually positive reactions had completely developed within sixty minutes. Results showed that the skin of old guinea pigs was less easily sensitized than the skin of young ones. In young and old guinea pigs, sites sensitized with antihorse guinea pig serum responded more actively to intracutaneous tests with horse serum than did sites sensitized with normal guinea pig serum. Comparing results in the above experiments, little difference was found in the percentage of old animals reacting to antigen introduced directly into the sites or into the abdomen. This indicates that the rate of absorption of horse serum was not a factor in the results. Histamine, in varying dilutions, was then injected intracutaneously on one side of the backs of young and old guinea pigs. On the other side, saline, with a pH approximately equal to the corresponding histamine dilutions, was injected. Reactions usually reached their height in thirty minutes. The ratios of the areas of the saline and histamine wheals, when compared in old and young guinea pigs, were about equal. The marked difference in the reactions obtained with antiprotein sera in the skins of old and of young guinea pigs could not be explained by differences in reactivity toward histamine in these two groups. B. SIEGEL.

Pharmacology and Physiology

Antihistamine Effect of Vitamin A and Allied Compounds. Balakhovsky, S. I., Borodotov, V. V., and Baldnitskava, S. V.: C. R. Acad. Sci. U.R.S.S. **54**: 243, 1946.

Various substances regarded as breakdown products of the vitamin A molecule have been shown to possess antihistaminic activity. Citral in a dilution

of 1:50,000 completely prevents the contraction of the isolated guinea pig intestinal strip ordinarily induced by one microgram of histamine. Geraniol, B-ionone, and pseudoionone show only slight antihistaminic activity. A colloidal solution of carotene, in both oxidized and unoxidized forms has strong histamine inhibiting action. Vitamin A itself, in a 1:15,000 dilution, exerts an antihistaminic effect, although this effect is not complete. The presence of an aldehyde group increases the antihistaminic activity of the substance. H.

Epidermal Sensitization to Streptomycin. Report of Six Cases Occurring in Twelve Nurses Handling the Drug. Strauss, M. J., and Warring, Jr., F. C.: J. Invest. Dermat. **9**: 99, 1947.

Four cases of contact dermatitis occurring in nurses who had frequently administered streptomycin over periods of from one to three and a half months, were described. All showed definitely positive patch reactions to streptomycin, and improved rapidly on avoidance of contact with the drug. Patch tests with streptomycin (1 Gm. in 5 ml.) on four normal individuals were negative. When patch tests with two different lots of streptomycin hydrochloride and a solution of streptomycin calcium chloride complex were done on twelve nurses who handled streptomycin, including the four cases described, six responded positively to all three test materials. This tended to rule out impurities in the drug as the offending agents. Of the six positive reactors, five had frequently contacted the drug, and one, only occasionally. Two had never experienced dermatitis, but nevertheless were advised to wear rubber gloves when handling the drug. In five of these six nurses, patch tests with dilutions of 1:5 to 1:100 of streptomycin showed positive reactions. At the dilution 1:500, only two demonstrated erythema, and at 1:1,000, only one. Controls with penicillin and tyrothricin were negative. For patch testing with streptomycin, a solution of one gram of the drug in 50 ml. of distilled water is recommended. B. SIEGEL.

Influence of Pyribenzamine and Antistine Upon the Action of Hyaluronidase. Mayer, R. L., and Kull, F. C.: Proc. Soc. Exper. Biol. & Med. **66**: 392, 1947.

A large group of albino rats were injected intracutaneously on the flank with mixtures of India ink and physiological saline and India ink and 1 per cent hyaluronidase solution. The size and intensity of the reactions were read in twenty hours. Larger reactions were noted with the hyaluronidase mixture. Twenty-four hours later, varying doses of Pyribenzamine or Antistine were injected subcutaneously. After twenty minutes, intracutaneous injections of the India ink mixtures were given on the opposite flanks of the animals. Both antihistaminic drugs restricted the spreading of the reactions obtained with both India ink mixtures. Guinea pigs were sensitized by the application of a 10 per cent paraphenylenediamine ointment. Three weeks later, solutions of antigen alone, and antigen-hyaluronidase were injected intracutaneously into two sites. The reactions at the hyaluronidase sites after twelve to sixteen hours were on the average seven times larger than at the antigen sites. Pyribenzamine given subcutaneously before the injection of these tests markedly reduced the size of both reactions. The results obtained in paraphenylenediamine sensitization experiments could not be reproduced with 2,4 dinitrochlorobenzene as the sensitizer. Similar experiments were carried out with procaine, a local anesthetic with low antihistaminic activity. This did not influence the normal spread of India ink mixtures except when large doses of procaine were used.

The fact that hyaluronidase enhances the size and intensity of allergic skin inflammations of the epidermal type and antihistaminics decrease this effect, suggests that hyaluronidase plays a role in epidermal sensitizations. It is possible that the antihistaminic drugs act in these conditions by their antihyaluroni-

dase effect. However it still remains to be experimentally demonstrated that hyaluronidase is actually liberated during the allergic reaction of the skin and that it bears any direct etiologic relationship with the reaction. B. SIEGEL.

Allergic Reactions to Penicillin. Gelfand, M. L.: New York State J. Med. **47**: 2707, 1947.

A woman with post-partum fever developed severe asthma, myalgia, arthralgia, subconjunctival hemorrhage, and a desquamating skin rash forty-eight hours after the primary administration of penicillin. Relief was obtained after withdrawal of penicillin and administration of Pyribenzamine. Direct and indirect skin tests with penicillin were negative. C.

The Pharmacology, Physiology, and Clinical Evaluation of the New Antihistaminic Drugs (Pyribenzamine and Benadryl). Arbesman, C. E.: New York State J. Med. **47**: 1775, 1947.

Pyribenzamine in daily doses of 100 to 400 mg. relieved 78 per cent of 461 patients with allergic rhinitis, 47 per cent of 159 patients with asthma, and 78 per cent of 199 patients with urticaria. No serious side effects were noted after daily administration of the drug over a two-year period. Pyribenzamine was found to be more effective and less toxic than Benadryl. C.

Antihistamine Drugs in Asthma and Hay Fever. Engelsher, D. L.: New York State J. Med. **47**: 1696, 1947.

One hundred ninety-three patients with asthma and hay fever were treated with Benadryl or Pyribenzamine for a three-day period. About two thirds of the patients were either unrelieved or aggravated, and of the remaining third, only 9 per cent were improved. None of the patients with severe asthma experienced any relief. Most of the beneficial effects were observed in urticarias. C.

A Comparison Between the Clinical Effects of Pyribenzamine and Those of Benadryl. Loveless, M. H., and Brown, H.: New England J. Med. **237**: 592, 1947.

Partial or complete control of symptoms was noted in over 80 per cent of 203 patients with acute urticaria or allergic rhinitis of pollen origin given. Pyribenzamine or Benadryl. Comparable results from each drug were reported by twenty-three of thirty-three patients given first one and then the other drug. Benadryl produced sedation in 60 per cent of patients. Patients whose efficiency and judgment may be impaired by sedation should be given Pyribenzamine for daytime use. Gastrointestinal complications followed Pyribenzamine more often than they did Benadryl. Mild to moderate constitutional reactions were diminished or disappeared twenty to thirty minutes after oral administration of the drug. Asthma was relatively refractory to the drugs as compared to nasal or cutaneous manifestations. Only partial improvement was noted in ten of twenty patients with asthma treated with these drugs. Completely negative results were obtained in four patients with atopic eczema. H.

Miscellaneous

The Allergen(s) of House Dust. Purification and Chemical Nature of Active Constituents. Rimington, C., Stillwell, D. E., and Maunsell, K.: Brit. J. Exp. Path. **28**: 309, 1947.

The character of the allergic substance obtained from different dusts did not differ materially so that the present studies were made with a single dust supply obtained mostly from carpets. "Crude house dust extract" was prepared by soaking the dust in 0.01 N. ammonia (1 liter to 1 Kg.). Twenty-four hours

later the liquid was manually expressed and the residue re-extracted for twenty-four hours. After centrifugation the both extracts were combined. The supernatant fluid was filtered through Kieselguhr, which clarifies the solution without producing any loss of activity. Sodium benzoate (20 Gm. per liter) was then added and hydrochloric acid (1 part conc. acid to 5 parts water) was stirred in until benzoic acid precipitation was complete. The precipitate was filtered and stirred with acetone (8 liters to 100 Kg.) to dissolve the benzoic acid. The insoluble material was covered, centrifuged, washed with alcohol, ether, and dried in vacuo. This crude antigen was fractionated with 25 per cent acetone and the precipitate, removed twenty-four hours later, was discarded. The acetone concentration was then raised to 75 per cent and the filtrate refractionated. This precipitate was washed with ether and alcohol, dried in vacuo and labelled "standard crude extract." This material contained 35 to 50 per cent ash (mostly sodium chloride, iron and aluminum), 20 to 39 per cent hexose, and 2 to 3 per cent nitrogen. Hydrolysis with acid yielded a galactose sugar and some simple amino acids.

Electrophoretic study at pH8 of the standard crude extract hydrolyzed with 0.5 N. sodium chloride revealed two main components, one immobile and colorless and the other mobile and associated with the color of the solution. Both these components showed a similar chemical composition and approximately equal potency when tested on dust sensitive patients.

The antigen in house dust is only a very small proportion of the total material, whose characteristics are due mainly to nonantigenic material. For testing and treatment 1 per cent solutions of the dust antigen, made up in 0.5 per cent carbol normal saline, were sterilized by immersion in boiling water for thirty minutes on each of three successive days. Heat at 100° C. is preferred to Seitz filtration since such treatment destroys filtrable viruses. Heated fractions give stronger intracutaneous reactions in dust-sensitive patients than do Seitz-filtered fractions. H.

The Allergen(s) of House Dust. Comparison With Products Derived From Moulds. Stillwell, D. E., Rimington, C., and Maunsell, K.: Brit. J. Exp. Path. **28**: 325, 1947.

Investigations were carried out with extracts of molds grown on pure cultures and with their culture fluids. Pooled extracts representing eight common genera were used. These extracts proved to be nonirritating when tested by the intracutaneous technique on fifteen nonallergics. Sixty-two patients with vasomotor rhinitis were tested with molds and house dust in a concentration of $10.^{-4}$ Fifteen of the forty-five found to be dust-sensitive also showed positive reactions to molds. All seventeen patients negative to dust also gave negative reactions to molds. In other words, no patient showed a sensitivity to molds and an insensitivity to dust.

A striking chemical similarity was noted between the three polysaccharide products derived from molds after hydrolysis and the dust antigen. All exhibited polypeptide-like grouping of simple amino acids associated with a polysaccharide complex. The usual color reactions for protein were not obtained. H.

The Allergen(s) of House Dust: Diagnosis and Desensitization of Dust-Sensitive Patients With "Crude Dust Antigen." Maunsell, K., Whetnall, E., and Rimington, C.: Brit. J. Exper. Path. **28**: 331, 1947.

Crude dust antigen (10 mg. to 10 ml. normal saline with 0.5 per cent phenol) was diluted serially with carbolsaline to give testing extracts of $10.^{-4}$ $10.^{-5}$ 10^{-6} concentrations. Of forty-nine subjects with no history of allergy none gave a threshold reaction with the 10^{-6} dilution, three reacted to 10^{-5} and

seventeen to the 10^{-4} dilution. Of ten subjects with a history of allergy, four exhibited threshold reactions to a dilution of $10,^{-6}$ three to $10,^{-5}$ and two to $10.^{-4}$ Twenty-nine (58 per cent) of the normal group were negative to the 10^{-4} dilution, whereas only one (10 per cent) of the allergic group failed to react with this concentration. Fifty-five of eighty patients with allergic symptoms showed positive reaction in a dilution of $10.^{-5}$ Forty-five patients were tested with dust $10,^{-5}$ cat, feathers, and molds. Thirty-five of these patients were positive to dust, twenty-two of these thirty-five were also found sensitive to one or more of the other allergens used for testing. No patient has been found who reacts to one of the other allergens but not to dust. Decrease of the threshold reaction to dust followed desensitization treatment. A blocking antibody was not found in the blood of patients desensitized with dust. H.

Diseases of the Collagen System. Klemperer, P.: Bull. N. Y. Acad. of Med. **23**: 581, 1947.

The author calls attention to the basic alteration found on histologic examination in certain diseases such as lupus erythematosus and scleroderma which he describes as diseases of the collagen system. Because the characteristic alteration, fibrinoid degeneration of collagen tissue, has been found in both lupus erythematosus and scleroderma, and also in periarteritis nodosa, these diseases have been considered to be of allergic origin. However, it is pointed out that collagen alterations identical with or hardly distinguishable from those seen in allergy may be produced experimentally, as by squeezing of the skin, or by acute bacterial infections or during orthostatic collapse in rabbits. Hence fibrinoid collagen alteration should not be interpreted solely and invariably as an expression of allergic reaction. C.

The Effect of Peptic and Tryptic Digestion on the Antigenicity of Trichinella Spiralis. Aikawa, J. K., Garrell, G. T., and Helsabeck, N. J.: J. Clin. Investigation **26**: 73, 1947.

Powdered Trichinella were subjected to alkaline-trypsin or acid-pepsin digestion under anaerobic conditions until the solutions were biuret-negative. Groups of dogs were then sensitized with these and with an undigested preparation. Intracutaneous and flocculation tests showed that the digested preparations retained their antigenicity. "The failure of proteolytic digestion to destroy the antigens suggests that the antigenic fraction of *Trichinella spiralis* is not solely a protein." It is suggested that proteolytic digestion of trichinella antigen employed for skin tests may reduce the incidence of false positive results. K.

Allergy Abstracts

Asthma and Hay Fever

Mold Fungi in the Etiology of Respiratory Allergic Diseases. V. Further Studies With Mold Extracts. Prince, H. E., Tatgi, G. E., and Morrow, M. B.: Ann. Allergy **5**: 435, 1947.

The activity of extracts of frozen, unwashed, lyophilized pellicles of *Alternaria tenius* and *Aspergillus niger* were compared with extracts of similarly prepared defatted pellicles and with extracts of washed, slowly-dried pellicles. Twenty-nine Alternaria-sensitive patients were scratch tested with Alternaria extracts in dilutions of 1:20 and tested intracutaneously with dilutions ranging from 1:100 to 1:100,000. No significant difference in skin reactivity could be discerned between the various Alternaria extracts. However, extracts of the culture broth were more reactive on scratch tests and on intracutaneous tests in dilutions of 1:1000 or greater. Similar results were obtained when Alternaria-sensitive patients were tested with pellicle and culture broth extracts of Aspergillus, although the incidence of positive reactions was less. Skin testing of Alternaria-sensitive patients with the dialysate and bag contents of dialyzed Alternaria and broth culture extracts indicated that skin-reactive fractions were retained within the bag. E. H. W.

The Tracheal Chain. I. A Preparation for the Study of Antispasmodics With Particular Reference to Bronchodilator Drugs. Castillo, J. C., and De Beer, E. J.: J. Pharmacol. & Exper. Therap. **90**: 104, 1947.

When the trachea of a guinea pig is sectioned into twelve muscular rings of approximately the same width and these rings are tied together with silk thread to form a chain, the minute changes brought about by bronchoconstrictor and dilator drugs are greatly magnified. The tracheal reactions parallel those of the bronchial muscles of the guinea pig. Epinephrine, aminophylline, and papaverine dilated the tracheal muscle, the effect being proportional to the dose used. Atropine, Novatropine, Syntropan, Trasentin, and Benadryl caused no relaxation, failed to relieve spasm induced by barium chloride, but did counteract the effect of acetylcholine. Benadryl in large doses caused contraction of the tracheal muscle despite the striking antagonism of this drug on the histamine-induced contraction. K.

Bronchial Asthma in Pulmonary Tuberculosis. Cohen, A. A.: Am. Rev. Tubere. **56**: 287, 1947.

Hospital charts of 7,301 patients discharged from a tuberculosis sanatorium over a ten-year period were reviewed to determine the incidence of bronchial asthma in tuberculous patients. All patients who ceased to have asthmatic attacks after admission or had typical attacks while in the sanatorium were excluded. Likewise, no patient was considered to have true bronchial asthma unless asthmatoid complications of tuberculosis had been ruled out by bronchoscopic examination. Fifty-five patients of the above series were considered to have true bronchial asthma, an incidence of 0.75 per cent which is lower than that reported among the general population. K.

Bronchography in Asthmatic Patients With the Aid of Adrenalin. Epstein, B. S., Sherman, J., and Walzer, E.: Radiology **50**: 96, 1948.

Bronchography in asthmatic patients was greatly facilitated by the subcutaneous administration of adrenalin. In sixteen patients with bronchial asthma accompanied by severe cough and expectoration, attempts at bronchography without the use of adrenalin were unsuccessful. Spasms of coughing occurred as the iodized oil entered the trachea and bronchus, and the oil was either expectorated or swallowed. Under fluoroscopic visualization none of the oil was seen to enter the swollen bronchi. However, when 0.5 to 1.0 ml. of a 1:1000 solution of adrenalin was injected subcutaneously, the secondary bronchi relaxed within half a minute and the oil could be seen entering and outlining the bronchial tree. The patients experienced little or no discomfort. Satisfactory bronchograms were obtained in fifteen of the sixteen patients and all showed radiologic evidence of bronchiectasis. J. SHERMAN.

Nethaphyl in the Treatment of Nasal Allergy and Bronchial Asthma. Hansel, F. K.: Ann. Allergy **5**: 397, 1947.

Nethaphyl, a combination of Nethamine (methylethylaminophenylpropanol) Hydrochloride and Butaphyllamine (theophylline aminoisobutanol) was administered to 750 patients with allergic bronchitis and bronchial asthma. Of these, 150 were children from 2 to 14 years of age. The majority of patients had nasal as well as bronchial symptoms. The results obtained in this series confirmed those reported by others on the use of theophylline compounds in the treatment of bronchial asthma. The average optimum dose varied from 3/8 of a grain of Nethamine and one-half of a grain of Butaphyllamine in children 4 to 12 years to twice that quantity for adults. When continuous adminstration was indicated the dose was repeated every three or four hours. Undesirable side effects were minimal and consisted of epigastric distress, nausea, vomiting, nervousness, and insomnia. Although Nethaphyl was administered as long as seven years in some instances, no tendency to increased tolerance was noted. Sensitivity to the drug was not encountered. E. H. W.

Intolerance to Common Drugs in Asthma. Prickman, L. E., and Morgan, J. L.: M. Clin. North America, July, 1947, p. 954.

Of seventeen consecutive patients hospitalized because of severe asthma, twelve either had an abnormal reaction to drugs administered in the hospital or gave a history of drug sensitivity. Seven patients in the group had reactions to more than one drug. Patients with true drug allergy responded to clinical or subclinical dosage by exhibiting allergic reactions, such as asthma or urticaria. Aspirin was the most common offender, five of the seventeen patients having been sensitive to it. All five patients had asthma, were sensitive to aspirin, and had nasal polypi, a triad frequently noted and usually associated with severe asthma and a poor prognosis. Intolerance and toxic effects following innocuous doses of drugs were also noted. A careful history of previous drug reactions should be sought in asthmatic patients. J. SHERMAN.

Dermatology

Skin Sensitization to BAL. Cornbleet, T.: J. Invest. Dermat. **9**: 281, 1947.

A case is described of dermatitis which developed on the palmar surfaces of the author's fingers following contact with a syringe used for the intramuscular injection of BAL. A patch test with 1 per cent BAL in peanut oil

was positive in six hours, the reaction reaching its maximum intensity in twenty-four hours. Patch tests with compounds related to BAL, with the other ingredients in the commercial product and with depilatories which were thought to be the original sensitizing agents all produced negative reactions. Passive transfer and scratch tests also produced negative results. It was concluded that the sensitization in this case was not to any particular fraction of BAL, but rather to the entire molecule. B. B. SIEGEL.

Otorhinology and Ophthalmology

Depth of Penetration of Nebulized Substances in the Respiratory Tree. Sloan, J. Q., Bain, G. F., and Brucer, M.: Proc. Soc. Exper. Biol. & Med. **66**: 264, 1947.

When penicillin aerosol is administered by spray into the oral cavity, the drug is partially absorbed by the pharyngeal mucosa and distributed throughout the body via the blood stream. A portion of the mist also follows the column of inspired air down the respiratory tree to exert a local surface action. On purely theoretical grounds it was concluded that large concentrations of aerosol mists could not penetrate deeply into the respiratory tree. However, the one experiment reported in the literature, which differentiated between the factors of pharyngeal absorption and of inspiratory penetration revealed that some of the nebulized substance actually did penetrate into the alveolar spaces. The following studies were done to investigate the apparent disagreement between the theoretical considerations and the experimental result.

A commercial nebulizer operated by handbulb was used to produce a sustained mist with droplets varying from 0.5 to 3 microns in size. When rats or mice were exposed to such a mist of 50 per cent India ink for sixty minutes and then sacrificed, carbon particles were found only in the nasopharynx and stomach. Another group of rats, rabbits, and dogs, under light anesthesia, was exposed by means of an oral cannula to mists of dilute India ink, gentian violet, or ferric ammonium sulfate, for from fifteen to sixty minutes. Only minute quantities of the nebulized substances were found in the trachea and bronchi, and none in the alveoli as seen in microscopic sections. When a tracheal cannula was used, larger deposits were found in the trachea and bronchi, but none in the smaller bronchioles or alveoli.

In other experiments the trachea and lungs were removed in toto and the tip was cut off from one of the lower lobes. The lungs were then artificially inflated by the nebulizer allowing a free flow of mist to pass through them. After fifteen minutes of inflating and deflating the lungs, only small amounts of material were found in the bronchi and none in the alveoli. With respirations stimulated by an intermittent mixture of CO_2 with dilute India ink mist for thirty minutes, carbon particles could not be found in the smaller bronchioles or alveoli. Using glycerolized carbon mist larger deposits were found in the tracheobronchial region, but generally, none in the alveoli.

It is concluded that in using commercial nebulizers the amount of nebulized substance reaching the trachea, bronchi, and bronchioles is not sufficient for therapeutic effectiveness. B. B. SIEGEL.

Inhalation of Penicillin Aerosol and Penicillin-Streptomycin Aerosol in Office Practice. Davis, D.: Arch. Otolaryng. **46**: 307, 1947.

The inhalation of penicillin aerosol and penicillin-streptomycin aerosol was found to be effective in relieving most simple infections of the respiratory tract. From 50,000 to 100,000 units of penicillin alone or combined with an equal

amount of streptomycin in one to two milliliters of propylene glycol were administered daily by aerosolization for from one to ten days. Patients with nasal allergy due to pollens or dust were not relieved unless the allergic condition was complicated by an infection and a purulent or muco-purulent secretion was present. Only patients with infectious asthma were benefited by aerosol therapy. Penicillin aerosol is a valuable adjunct in the treatment of acute and chronic respiratory infections. C.

A Simplified Technic of Treating Sinusitis With Penicillin Aerosol. Barach, A. L., Rumsey, C. C., Soroka, M., and Rader, D.: New York State J. Med. **47**: 1498, 1947.

A simplified technique is described for producing negative pressure during nasal inhalation of penicillin aerosol for the treatment of acute and chronic sinusitis. An automobile pump permits economical nebulization of the penicillin aerosol, either for oral inhalation of the drug or in conjunction with negative pressure during the nasal inhalation of penicillin. Effective penicillin blood levels were demonstrated after inhalation of 50,000 units per cubic centimeter in normal saline by this method. C.

Miscellaneous Allergies

Allergic Carditis, Pericarditis and Pleurisy. Report of a Case of Serum Sickness With Predominant Cardiac Manifestations and Symptomatic Recovery. (Preliminary Report.) McKinlay, C. A.: Lancet **68**: 61, 1948.

A 21-year-old male who several years previously had received routine inoculations while in the Navy developed accelerated serum sickness with a febrile reaction and erythema five hours after the injection of tetanus antitoxin. The patient complained of weakness, nausea, vomiting, chills, precordial pain, and dyspnea. The precordial pain persisted and twenty-three days following the onset of the condition cardiac enlargement and an apical systolic murmur were noted for the first time. On the thirty-fourth day of the illness a precordial friction rub appeared along with further cardiac enlargement. Transient urticaria developed. On the thirty-fifth day a pleurisy with effusion was detected. Within the next six days, however, all signs and symptoms had disappeared and the heart had returned to normal size. The eosinophile counts ranged between 1 and 7 per cent. The sedimentation rate was increased. A positive heterophile antibody reaction in a dilution of 1 to 64 was found during the late stages of the illness. Antihistaminic drugs were not used in the treatment of the condition. F.

Tubercle Bacillus Antigens—Biological Properties of Two Substances Isolated From Paraffin Oil Extract of Dead Tubercle Bacilli. Choucroun, N.: Am. Rev. Tubere. **56**: 203, 1947.

Dead whole tubercle bacilli injected with paraffin oil are far more antigenic than the same bacilli in saline solution. Previously this was assumed to be due to increased tissue vulnerability secondary to the inabsorbable oil medium. Studies are reported which show that the mechanism by which the paraffin oil enhances the antigenicity of dead tubercle bacilli is by removing the antigenic substances from the bacilli. Dioxane precipitated an antigen from the oil extract of tubercle bacilli which induced hypersensitivity to tuberculin and lesions identical with those produced by injections of whole bacilli in paraffin oil in guinea pigs. A chloroform extract of the dioxane precipitate

appeared to be very toxic to the animals. This toxic fraction was found to be a polysaccharide ester of mycolic acid. "This carbohydrate-lipid complex has the remarkable capacity of producing lesions in the lungs when injected into guinea pigs intraperitoneally, in paraffin oil. Such lesions are observable microscopically ten days after injection, even when the amount inoculated is as small as one gamma." These lesions were unlike those produced by paraffin oil, mycolic acid, or polysaccharide alone.

The sensitizing fraction was separated from the toxic fraction and was identified as a protein capable of establishing cutaneous tuberculin hypersensitivity in normal guinea pigs. Animals sensitized with this protein reacted to whole intact bacilli with the typical delayed inflammatory reaction. The hypersensitivity remained for many months. The intraperitoneal injection of old tuberculin made these animals sick for twenty-four hours but did not kill them as it does tuberculous animals. Passive transfer of hypersensitivity was unsuccessful when serum alone was used but was accomplished in two of ten trials when 4 to 5 ml. of fresh whole blood was injected into normal animals. In three of twelve trials passive transfer of hypersensitivity was accomplished through the use of extracts of lung and spleen tissue taken from hypersensitized guinea pigs. The tuberculin test was carried out on the recipient animals thirty-six hours after these injections.

Five series of experiments were carried out on guinea pigs to correlate the antigenic fractions obtained with immunity to tuberculous infection. The "sensitizing" fraction failed to enhance resistance to tuberculosis. Preliminary investigation of the "toxic" chloroform-soluble, carbohydrate-lipid fraction indicated that this fraction enhanced resistance to tuberculous infection. The survival time was increased in four guinea pigs which had been immunized with both the protein sensitizing fraction and the "toxic" fraction.

The carbohydrate component of the "toxic" fraction when separated from mycolic acid was a strong antigen which gave specific precipitin reactions with sera of rabbits and guinea pigs immunized by the whole oil extract, and also with the sera of animals which had been immunized by the "toxic" carbohydrate-lipid complex alone. Titers sometimes ran as high as 1:10,000,000. Strong precipitations were also obtained with the serum of a horse which had been immunized with whole tubercle bacilli and with the sera of rabbits immunized with human and avian tubercle bacilli. A homologous carbohydrate-lipid could also be extracted from bovine bacilli and *Bacille calmette guérin*. This indicated that type-specificity analogous to that for pneumococci is not conferred on tubercle bacilli by their carbohydrates. E. K.

Streptomycin Sensitivity. Development of Sensitivity in Nursing Personnel Through Contact During Administration of the Drug to Patients. Rauchwerger, S. M., Erskine, F. A., and Nalls, W. I.: J. A. M. A. **136**: 614, 1948.

Sensitivity to streptomycin developed in six nurses who had handled the drug intermittently for periods of from eight to eighteen months. The reaction was characterized by an initial erythema followed by severe pruritus and a papulovesicular eruption which in two instances caused denudation of the skin of the thumbs and index fingers.

Intracutaneous skin tests established that latent sensitivity may exist. The tests were carried out on a group of controls and on ninety-seven nurses who had handled the material. Positive twenty-four-hour reactions were observed in seven of the nursing staff and doubtful reactions occurred in six others. Patch tests were performed on only three nurses. Two showed positive reactions in twenty-four hours, while the third nurse who was taking Pyribenzamine for

a severe pruritus during the test period gave a negative reaction. Three days after the Pyribenzamine was discontinued the patch test in this patient became strongly positive. The authors believe that the patch test gives inconsistent results because of difficulty in regulating the concentration of the test material. They have adopted a routine of testing personnel intracutaneously every four months in an attempt to detect early cases of sensitivity. Prophylactic measures such as wearing rubber gloves, washing before and after handling the streptomycin and the syringes used in its administration were instituted. Contact through nebulization during steam sterilization of syringes was avoided. F.

Histoplasmin Sensitivity: Results of Studies of Children in Alabama. Welch, S. W., and Berrey, R.: Am. J. Dis. Child. **74**: 607, 1947.

A survey was made in Birmingham, Alabama, of the incidence of skin reactions to tuberculin (O.T. 1:1000) and to histoplasmin (1:100 dilution). Of 1,200 Negro children 15 per cent reacted to histoplasmin, and 19 per cent to tuberculin. Of 923 white children from families having relatively high incomes, 4.4 per cent showed positive reactions to histoplasmin and 8.34 per cent to tuberculin. Two cases of clinically active histoplasmosis were discovered in the series. E. K.

Serum Sickness Due to Crystallized Bovine Albumin. Heyl, J. T., and Janeway, C. A.: J. Clin. Investigation **26**: 1185, 1947.

Sixty subjects each received 25 Gm. of crystallized bovine serum albumin intravenously. Twenty-four developed serum sickness of variable severity characterized by a long incubation period (ten to thirty-three days) and accompanied by purpura, signs of hepatic and renal damage, and cardiac symptoms with electrocardiographic changes. One subject died and at autopsy was found to have necrosis of the myocardium. Immunologic studies indicated that the albumin was a poor antigen for the production of precipitin or skin sensitizing antibodies. The albumin disappeared very slowly from the circulation in normal individuals but in certain patients who developed serum disease its disappearance was rapid. However, "in some cases of severe serum sickness, recovery occurred before the disappearance of the bovine albumin from the circulation and antibodies never appeared." K.

The Effect on the Trichinella Skin Test of Simultaneous Infection With Bovine Tuberculosis in Trichinous Rabbits. Harrell, G. T., and Helsabeck, N. J.: J. Clin. Investigation **26**: 69, 1947.

Either virulent bovine tuberculosis or trichinosis or both were induced in groups of rabbits. Thirty-nine days after the infection was initiated intracutaneous tests were carried out with trichina antigen and tuberculin. At forty-five days the animals were sacrificed and the degree of infection with tuberculosis or trichinae was estimated. Tuberculosis did not affect cutaneous reactivity to trichinella antigen. Four animals with proved trichinosis failed to react to the 1:200 trichinella cutaneous test. K.

Production of Allergic Gastric and Duodenal Edema Which Predisposes to the Histamine-Provoked Ulcer in Dogs. Friesen, S. R., State, D., Jasper, D. E., Finn, M., and Wangensteen, O. H.: Surgery **23**: 167, 1947.

Edema of the stomach and duodenal wall of dogs was experimentally produced by local passive sensitization of the stomach and duodenal wall with immune serum followed by intravenous injection of specific antigen. Three of six

dogs showed ulcers at the site of the edema. Twelve dogs, who in addition received injections of histamine-in-beeswax, all developed ulcers in the edematous area. Two dogs died of peritonitis following perforation of the ulcers.

Ulcers were thus produced by local antigen-antibody reaction alone but were provoked more readily with the concomitant administration of histamine. Ulcers could not be produced by daily injection of histamine alone.

Local anaphylactic edema may therefore be a factor in the production of gastrointestinal ulcer. J. SHERMAN.

Anaphylaxis

Experimental Aspects of Penicillin Sensitization. II. With Reference to the Schultz-Dale Phenomenon. Cormia, F. E., Lewis, G. M., and Hopper, M. E.: J. Invest. Dermat. **8**: 395, 1947.

The possible relationship between sensitization to penicillin and superficial fungous disease was studied. Eight guinea pigs were sensitized with *Trichophyton gypseum* by repeated intracutaneous injections. When eleven of their uterine horns were tested in the Dale bath with sufficient amounts of either commercial sodium penicillin or crystalline sodium penicillin G, maximum contractions were obtained in two tests and delayed reactions in three. With commercial trichophytin an anaphylactic response occurred in only one of eleven tests with a partial response in another. Twelve guinea pigs were then sensitized by single intracutaneous or repeated intraperitoneal injections of either commercial or crystalline sodium penicillin. The fifteen uterine horns of the animals tested gave two anaphylactic responses to penicillin with three partial or incomplete reactions. When treated with commercial trichophytin, penicillin-sensitized uterine horns reacted partially in two cases of fifteen. In three of the four instances in these experiments where positive Trichophyton reactions were obtained, uterine contractions were also obtained with penicillin. Control experiments with nonsensitized uterine horns elicited no reactions with either penicillin or Trichophyton. It is concluded that guinea pigs can be sensitized with about equal frequency to commercial and crystalline sodium penicillin about 50 per cent of the time. The anaphylactic responses in these guinea pigs were generally partial, incomplete, and delayed, suggesting that penicillin is an imperfect allergen. On the basis of the above experiments it is further concluded that there is a common antigen in penicillin and *T. gypseum*. This supports the theory that shock-like reactions in man following penicillin administrations are caused by pre-existing sensitization by pathogenic fungi.

B. SIEGEL.

Antiproteins in Horse Sera. II. Antibodies to Pneumococcus Nucleoprotein and Their Reaction With Antigen. Heidelberger, M.: J. Exper. Med. **86**: 77, 1947.

Antitoxins are characterized by their narrow zone of specific precipitation with toxin (as in the Ramon flocculation titration). This zone corresponds to the equivalence zone of the precipitin reaction. The precipitin reaction, however, shows no inhibition in the zone of antibody excess. Crystallized egg albumin and hemocyanin were used to induce antibody formation in the horse. The resultant antibodies gave the antitoxic pattern of flocculation with antigen. Pneumococcus polysaccharide which is known to elicit a precipitin type of antibody was tested in the horse. Whole and autolyzed pneumococci derived from a pleural exudate were injected intravenously. The antibody induced

by this means showed a precipitin type of reaction with pneumococcus nucleoprotein rather than the antitoxin type of response. E. K.

Antiproteins in Horse Sera. III. Antibodies to Rabbit Serum Albumin and Their Reaction With Antigen. Treffers, H. P., Heidelberger, M., and Freund, J.: J. Exper. Med. **86**: 83, 1947.

The subcutaneous injection of alum-precipitated rabbit serum albumin into two horses resulted in the appearance of an antibody which resembled horse diphtheria antitoxin in "giving a sharp zone of flocculation with antigen, in being water-soluble, in reactivity toward an anti-antibody rabbit serum and in its electrophoretic properties." The same antigen administered intravenously to horses did not produce precipitable antibody. Quantitative data on the antigen and antibody nitrogen present in the precipitates under various conditions of volume and temperature are included. K.

Granuloma, A Characteristic "Qualitative" Change in Focal Anaphylactic Inflammation. Goddard, J. W.: Am. J. Path. **23**: 943, 1947.

Sensitized guinea pigs were injected subcutaneously with the sensitizing antigen in order to study the nature of the local reaction, the focal anaphylactic reaction of the Arthus type. The reticulo-endothelial cells, the histiocytes, and monocytes of the subcutaneous tissue took part in this reaction. The characteristic lesion was agranuloma, circular or ovoid in outline, consisting mainly of histiocytes with an intermingling of lymphocytes, plasma cells, and eosinophiles. Giant cells were sometimes present at the periphery. Granulomata sometimes developed in or around adipose lobules or perineurally, but were most often perivascular. The reacting histiocytes were derived from the endothelial and perithelial cells of regional capillaries. Involution of the granuloma occurred by fibrosis followed at times by mucoid or myxomatous degeneration.

J. Sherman.

Pharmacology and Physiology

Pathogenesis of Glomerulonephritis and Rheumatic Fever. In Vivo Activation of Tissue Antigens as a Result of Streptococcic Infection and Consecutive Formation of Autoantibodies. Cavelti, Philip A.: Arch. Path. **44**: 119, 1947.

Rats were focally infected with Group A beta hemolytic streptococci causing inflammatory reactions and, in a few instances, abscess formation. Sera taken from these rats from twelve to thirty-six hours after the initiation of the infection showed the presence of autogenous tissue antigens when tested with the sera of rabbits immunized against rat kidney, heart, and connective tissue. Since the tissue specificity of the rabbit antisera was not high, it was not possible to determine which tissues yielded the autoantigens.

Sera obtained from the same rats from eight to fourteen days after the onset of the infection showed the presence of autoantibodies when tested with extracts of rat kidney, and heart.

It is thought that during streptococcic infection autogenous tissue antigens may be formed by the action of the organism or its toxin on the tissues of the host. As a response to antigenic tissue-streptococcic combinations autoantibodies are formed, the pathogenic effect of which may cause the development of renal and cardiac lesions. J. Sherman.

The Altered Response of Human Beings to the Intramuscular Administration of Typhoid Vaccine During Massive Salicylate Therapy. Jager, B. V., and Nickerson, M.: Am. J. Med. **3**: 408, 1947.

The parenteral administration of typhoid vaccine in normal subjects usually results in the production of circulating antibodies to this organism. In addition, there is a transient rise in the plasma fibrinogen, the erythrocyte sedimentation rate, and total leucocyte count, as well as a transient decrease in total lymphocytes. Immediately following the injection of the vaccine a rise in serum gamma lobulin occurs which soon returns to its original level.

In patients receiving massive doses of salicylates the changes occurring after administration of typhoid vaccine differed strikingly from those noted in the controls. Local reactions were milder. No significant rise in the plasma fibrinogen, the total leucocyte count, or the total number of granulocytes occurred. No immediate or delayed rise in gamma globulin developed, antibody production appeared to be impaired significantly. Two subjects with rheumatic fever who were not treated with salicylates developed antibody titers as high as healthy control subjects. It is possible that the salicylates in some way modify the antigenicity of the bacterial proteins. Another possibility is that in such patients the reticulo-endothelial system more rapidly removes the antigen from the circulation and another may be diminished antibody response caused by impaired production of antibody by lymphocytes. HARTEN.

The Alleged Excretion of Histamine in Parathyroidectomized Dogs. Misrahy, J., and Salama, S.: Am. J. Physiol. **150**: 420, 1947.

Parathyroidectomized dogs showed no increase in the amount of histamine excreted in the urine. The postoperative urinary histamine gradually declined or was maintained at the preoperative level until shortly before death at which time a rapid drop was the rule. F.

Serological Response to Intranasal Administration of Inactive Influenza Virus in Children. Quilligan, J. J., Jr., and Francis, T., Jr.: J. Clin. Investigation **26**: 1079, 1947.

Inactivated influenza A and B virus solution was administered in a fine intranasal spray or subcutaneously to groups of institutionalized children. Agglutination-inhibition titrations of chicken red blood cells were carried out on pre- and post-treatment specimens of sera. Subcutaneous vaccination resulted in a higher and more persistent antibody response than intranasal inoculation although the latter was effective in elevating antibody levels. K.

Miscellaneous

Relation of the Adrenals to Immunity. White, A.: Bull. New York Acad. Med. **24**: 26, 1948.

The adrenal cortex is one of the hormonal factors involved in immunity. The accelerated release of adrenal cortical hormones as a result of one of a number of stimuli such as heat, cold, tissue injury, injections of foreign proteins, histamine, insulin, epinephrine, etc., increases the output of pituitary adrenotrophic hormone with a resultant increase in the concentration of circulating adrenal cortical steroid hormones. These influence the development of phagocytic cells and the production of immune globulin. They also have a marked effect on reticulo-endothelial cells long known to be concerned with processes

of immunity. Injection of adrenal cortical steroids or increased secretion of these hormones as a result of pituitary adrenotrophin injection produces an elevation of antibody titer either in a hyperimmunized animal or in a previously immunized animal with no circulatory antibody. This suggests that the physiologic basis of the anamnestic response is the pituitary-adrenal cortical control of lymphocyte structure and function. This control over the contribution of the lymphocyte to immune globulin production is related to a specific type of resistance, immunity based on antibody formation. C.

The Lymphoid Tissue and Antibody Formation. Murphy, J. B., and Strum, E.: Proc. Soc. Exper. Biol. & Med. **66**: 303, 1947.

Adrenalectomized and normal rabbits were sensitized by intraperitoneal injections of 10 ml. of horse serum and bled ten days later. The sera from the adrenalectomized rabbits showed much higher precipitin titers than the control animals. Rabbits whose adrenals had been removed two to three weeks previously and intact rabbits were sensitized by five intravenous injections of 1 ml. of horse serum at two-day intervals and bled after ten days. Even higher precipitin titers were obtained in these adrenalectomized animals than in the previous experiment. The control rabbit sera averaged about the same titers. It was also found that adrenalectomized rabbits produced higher agglutinin titers to heated saline suspensions of *Salmonella enteritidis* than did intact animals.

Rabbits were injected daily for twenty-three days with adrenal cortical hormones immediately following adrenalectomy. These animals, untreated adrenalectomized, and normal animals were sensitized with horse serum as in the original experiment. There was no appreciable difference found in the precipitin titers of hormone treated and untreated adrenalectomized rabbits.

It is concluded that following adrenalectomy in rabbits a hypertrophy of the lymphoid tissue develops and results in an enhanced ability to produce antibodies. However, prevention of the adrenal cortical hormones does not reduce this ability. Under these circumstances the high titers may result from the destructive action of these hormones on the lymphocyte with a release of large amounts of the antibodies. B. SIEGEL.

Fluorescein as an Indicator of Antihistaminic Activity: Inhibition of Histamine-induced Fluorescence in the Skin of Human Subjects. Bukantz, S. C., and Demmin, G. J.: Science **107**: 224, 1948.

Intradermal fluorescein was employed as an indicator to determine the effect of antihistaminics upon changes in capillary permeability which follow the injection of histamine. Initial experiments demonstrated that normal rabbit skin was not a suitable test organ for these experiments. In the normal skin of humans and dogs it was demonstrated that histamine injected intradermally increased capillary permeability as evidenced by the fluorescein technique and that the antihistaminic drugs decreased this effect. In the one allergic individual studied it was found that the intradermal fluorescein sites and the fluorescein-histamine sites remained visible for equal periods, indicating the likelihood of a local release of histamine or a histamine-like substance at the fluorescein site. The site prepared with a combination of fluorescein, histamine, and Benadryl remained visible for a much longer time, indicating the neutralizing effect of the antihistaminic drug. It is anticipated that the application of the dermofluorometer to these studies will yield time intensity curves permitting accurate bio-assay of histamine and antihistamine drugs and may

further provide a useful tool for the investigation of the degree and duration of humoral and tissue antihistaminic properties following different routes of administration of various antihistaminic drugs. F.

Effects of Rutin on Permeability of Cutaneous Capillaries. Ambrose, A. M., and De Eds, F.: J. Pharmacol. & Exper. Therap. **90**: 359, 1947.

Rutin administered intravenously to rabbits in doses of 100 or 200 mg. per kilogram decreased the cutaneous capillary permeability of these animals as shown by the trypan blue test. Capillary permeability was induced by chloroform applied locally, histamine injected intravenously, and by the application of suction. The period of effectiveness of the Rutin started ten minutes after its injection and lasted ninety minutes. E. K.

Some Pharmacological Properties of Rutin. Wilson, R. H., Mortarotti, T. G., and De Eds, F.: J. Pharmacol. & Exper. Therap. **90**: 120, 1947.

Verification of Rutin's protective action on epinephrine was obtained by in vitro studies with guinea pig colon. Relaxation of the colon induced by epinephrine was prolonged in direct proportion to the dose of Rutin added to the preparation. Rutin itself did not cause relaxation except irregularly when high doses were employed. Rutin did not alter the response of the strip to histamine or acetylcholine. When guinea pigs were injected with Rutin ten to thirty minutes prior to the administration of shocking doses of histamine, the percentage of animals that survived was increased. When the interval between the administration of the two drugs was increased or when both were mixed and injected together, no such protection was demonstrable. It is suggested that the protection which is afforded in the above experiments may be due to a slight increase in circulating epinephrine as a result of in vivo retardation of epinephrine destruction. E. K.

A Comparison on Some Anti-histamine Substances. Graham, J. D. P.: J. Pharmacol. & Exper. Therapy **91**: 103, 1947.

Anthisan, also known as 2786 R.P., Benadryl, and Antistine were compared as to their effectiveness in counteracting the action of histamine on the blood pressure of cats, on the isolated intestine of guinea pigs, and on the bronchi of intact guinea pigs. In the cat depressor test, 2786 R.P. was the most effective and Benadryl the least. When the isolated guinea pig ileum or the bronchus of the intact guinea pig was used as test organs, 2786 R.P. was the most potent and Antistine the least. None of these drugs suppressed the formation of gastric juice but 2786 R.P. was more active than the other two in this respect. All three drugs failed to modify histamine inhibition of isolated uterine muscle in the rat.

Toxicity studies in mice indicated that Benadryl is somewhat more toxic than the other two drugs. Anthisan is a more violent central nervous system stimulant than Benadryl, while Antistine is a depressant and kills by respiratory depression. It was noted that 2786 R.P. which was the most potent antihistaminic was also the most active local anesthetic. K.

Fatal Reactions to Intravenous Administration of Aminophylline. Report of Three Cases. Bresnick, E., Woodard, W. K., and Sageman, C. B.: J. A. M. A. **136**: 397, 1947.

Three fatal reactions following the intravenous administration of aminophylline were observed. All three of the patients were critically ill, two with

acute coronary occlusions and the third with uremia, myocardial damage and acute pulmonary edema. The deaths occurred very suddenly during slow administration of the aminophylline. The mode of death suggested cardiac standstill or ventricular fibrillation.

Aminophylline, in addition to being a coronary vasodilator, has a stimulating effect on the myocardium and increases cardiac action. The increase in metabolic demands on the myocardium which occurs after the administration of aminophylline may be greater than can be compensated for by the vasodilating effect of the drug, thus precipitating coronary insufficiency. The reactions appear to be unrelated to the total dose administered since the fatalities followed the administration of from 0.1 to 0.36 Gm. of the drug. F.

The Quantitative Estimation of Theophylline in Blood. Truitt, E. B., Jr., Carr, C. J., Bubert, H. M., and Krantz, J. C., Jr., J. Pharmacol. and Exper. Therap. **91**: 185, 1947.

A colorimetric method for the assay of theophylline in blood is described. Samples of blood with known added amounts of theophylline ranging from 0.20 to 0.80 mg. per cent were subjected to this analysis and the error of determination fell within ±0.04 mg. Blood levels of eight patients receiving 1 to 2 Gm. of theophylline sodium aminoacetate daily ranged from 0.23 to 1.8 mg. per cent. K.

The Relative Pressures Within Cutaneous Lymphatic Capillaries and the Tissues. McMaster, P. D., J. Exper. Med. **86**: 293, 1947.

Direct measurement of pressure within cutaneous lymphatic capillaries of normal mice revealed pressures ranging from 0.– to 2.7 millimeters of water. The pressure of the interstitial fluid in adjacent tissue was measured by the pressure necessary to inject a poorly-absorbable dye solution. The tissue pressure equaled or exceeded intra-lymphatic pressure to produce edema, the intralymphatic capillary pressure was increased. The tissue pressure, however, was so much increased by the edema that the gradient between tissues and capillaries sometimes reached as much as 5.9 milliliters of water. This indicates that a pressure gradient is important in lymph formation, both under normal and pathological circumstances. E. K.

Allergy Abstracts

Asthma and Hay Fever

The Effect of Drugs in Modifying the Response of Asthmatic Subjects to Inhalation of Pollen Extracts as Determined by Vital Capacity Measurements. Schiller, I. W., and Lowell, F. C.: Ann. Allergy **5**: 564, 1947.

The capacity of aminophylline, epinephrine, atropine, and Pyribenzamine to prevent the decrease in vital capacity which results from the inhalation of an aerosolized pollen extract was investigated in three patients. Aminophylline was administered intravenously in a dose of 0.48 Gm., epinephrine, subcutaneously in doses of 0.3 to 0.5 ml., Pyribenzamine, intravenously in a dose of 0.6 to 1.2 milligrams. Aminophylline provided the greatest protection; epinephrine gave definite but incomplete protection; atropine and Pyribenzamine were totally ineffective. Aminophylline administered intravenously, Isuprel inhaled in 5 per cent concentration, and epinephrine were effective, in decreasing order, in restoring the reduced vital capacity resulting from the inhalation of pollen extract. Atropine and Pyribenzamine were ineffective in this respect. However, atropine decreased the response to Mecholyl and Pyribenzamine protected against the inhalation of histamine and restored the vital capacity reduced by the inhalation of histamine. These results suggest that neither acetylcholine nor histamine are determining factors in the production of pollen-induced asthmatic attacks. E. H. W.

Active Sensitization to Pollen. Wodehouse, R. P.: Ann. Allergy **5**: 558, 1947.

During the course of a series of local passive transfer experiments, four of forty-seven subjects became skin-sensitive to ragweed pollen. All four had shown negative reactions to ragweed extract at the beginning of the experiments. Three of these four individuals gave a positive family history of allergy. Two of the three gave a history of food urticaria and one had dermographism. The fourth subject gave a history of vasomotor rhinitis during the summer. Two of the subjects showed positive skin reactions to allergens other than ragweed. Although a number of different pollen extracts were used in the experiments, skin sensitivity was induced only to ragweed. The total dosage of ragweed pollen administered varied from 14.3 to 120 units. Three of the subjects were sensitized in less than a year and the fourth became skin-sensitive within fourteen months. None developed clinical sensitivity within the period of observation. Apparently all the subjects "were on the road to sensitization from their natural exposure to ragweed pollen, and the injections of pollen served only to accomplish the last step." It appears that it is extremely difficult to sensitize human beings to pollen by injection unless they are inherently atopic and the pollen used is one to which they are annually exposed. It is not stated whether the positive reactions were transferable. E. H. W.

Mold Fungi in the Etiology of Respiratory Allergic Diseases. VII. Further Survey Studies. Morrow, M. D.: Ann. Allergy **5**: 442, 1947.

A mold survey was made of the United States. Data was collected at thirty-one stations which participated for varying periods of time up to six years. The

mold culture plate technique was employed. At each station, four plates were exposed every month, two plates each at two exposure dates. At all stations, the following molds were among the "top ten": Alternaria, Hormodendrum, Penicillium, Aspergillus, Pullularia, Sterile pale species, Sterile dark species, Torula, Fusarium, Trichoderma. At five stations studied for the qualitative mold picture, the "big six" for each station were as follows: At Buffalo, Alternaria, Sterile pale species, Hormodendrum, Penicillium, Torula, Pullularia; at Decatur, Illinois, Alternaria, Aspergillus, Penicillium, Hormodendrum, Sterile pale species, Pullularia; at Memphis, Hormodendrum, Alternaria, Sterile pale species, Penicillium, Aspergillus, Pullularia; at Galveston, Alternaria, Hormodendrum, Sterile pale species, Penicillium, Aspergillus, Pullularia; at Pittsburgh, Sterile pale species, Alternaria, Hormodendrum, Pullularia, Penicillium, and Aspergillus. E. H. W.

Mold Fungi in the Etiology of Respiratory Allergic Diseases. VIII. Mold Allergy in West Texas—Clinical Observation. Sellers, E. D., and McKenzie, E.: Ann. Allergy **5**: 455, 1947.

During a five-year period, 392 patients with inhalant allergy in Abilene, Texas, were tested with mold extracts by the intracutaneous technique. Extracts of Alternaria, Aspergillus, Curvularia, Fusarium, Helminthosporium, Hormodendrum, Spondylocladium, and Penicillium were employed. Of the 392 patients, 44.3 per cent reacted positively to one or more mold extracts. Thirty-three, or 8.4 per cent, reacted to molds only, and 141, or 35.9 per cent, reacted to molds and other inhalant extracts. Among these inhalant-sensitive patients, 14.7 per cent with asthma and 17.6 per cent with hay fever reacted to molds. Thirty-one patients with both asthma and hay fever as well as sixteen with other forms of respiratory allergy were found to be mold-sensitive. Mold sensitivity was particularly prevalent in patients under 20 years of age. Twenty-one of thirty-three patients sensitive only to molds and 49.4 per cent sensitive to molds and other inhalants were treated successfully. E. H. W.

Initial Symptoms of Pollenosis at an Advanced Age. London, M.: Ohio State M. J. **44**: 489, 1948.

An 85-year-old woman gave a history of having developed clinical symptoms of ragweed hay fever for the first time at the age of 83. She had lived in a ragweed area for forty-seven years prior to the onset of the symptoms. She showed positive reactions to ragweed pollen, dust, wheat, flaxseed, and grass pollen. She gave a positive reaction to ragweed pollen on passive transfer. F.

Dermatology

Studies on Eczematous Sensitization. I. The Route by Which the Sensitization Generalizes. Rostenberg, A., Jr.: J. Invest. Dermat. **8**: 345, 1947.

Guinea pigs were sensitized simultaneously with acetone solutions of 2:4 dinitrochlorobenzene and paranitrosodimethylaniline, either by intracutaneous injection, or by dropping the solution directly on the skin of the flank. At six, twelve, or twenty-four hours after sensitization elliptical skin islands were made on one of the flanks with incisions penetrating down to the underlying muscle layer. Precautions were taken to prevent union between the island and surrounding epidermis. Nine days following the sensitizing application, areas on the island site and on the opposite flank were tested with each chemical. Tests were read after twenty-four and forty-eight hours. Results revealed that twenty-six of thirty-four tests were positive off the island as against twenty of

thirty-four on the island, regardless of the original site of sensitization. The time at which the island was made did not seem to affect the results. With 2:4 dinitrochlorobenzene the allergen crossed in either direction in fourteen of seventeen trials and with paranitrosodimethylaniline in only nine of seventeen trials. Six animals reacted only to one of the chemicals off the island, but not to the same chemical on the island. Three animals reacted positively on the island but negatively off the island. Thus, the operative procedure did not seem to interfere with the generalization of the sensitization, except that the island site was sensitized less often irrespective of the site of original application of the allergen. This is attributed to the fact that during the first six hours all routes for dissemination of the excitant were intact, and after the formation of the island the hematogenous and some deep lymphatic routes were still functioning. It is thought that in eczema, the sensitizing antigen is converted at the site of contact into a conjugated or modified allergen which is spread mainly via the lymphatics. B. SIEGEL.

The Histamine Content of Normal and Diseased Skin. Ottolenghi, L.: Gior. ital. Dermat. e sif. **87**: 153, 1946.

The author had previously demonstrated that the estimation of the histamine content of bullae was a more satisfactory procedure than that of the whole skin tissue. Therefore, he measured the concentration of histamine or histamine-like substances in bullae artificially produced in patients suffering from various diseases and compared them with bullae raised on normal skin areas in the same subject. In eczema there was a marked difference in the histamine content of bullae raised on the involved skin as compared with those on normal skin. In urticaria the difference was much less. In lupus vulgaris and in secondary syphilis the differences were less than in eczema, and in psoriasis the discrepancies were minimal. The highest titres were obtained in erythrodermia. It is concluded that in a number of skin diseases an important part is played by the production or concentration of histamine and histamine-like proteins. C.

Kaposi's Varicelliform Eruption. Relation to Atopic Dermatitis. Unger, L.: Ann. Allergy **5**: 426, 1947.

Kaposi's varicelliform eruption was observed in a 19-year-old female. The patient who had been treated for atopic dermatitis and hay fever for nine years developed a sore throat and received sulfa drugs every three hours. A generalized papular rash developed and the drug was discontinued after two days. Temperature up to 105° F., prostration, nausea, vomiting, bloody diarrhea, hematuria, delirium, and stupor followed. At the height of the illness, the skin of the neck was deeply pigmented and hyperkeratotic, swollen, and oozing. Pearly umbilicated vesicles 5 to 7 mm. in diameter were present on the face, neck, arms, upper chest, and in the groins. Palms, soles, and mucous membranes were not involved. The patient ran a stormy course until the eleventh day when her temperature dropped by crisis. At the end of her illness the lichenified, flexural dermatitis persisted but the vesicles had disappeared without scarring. The virus of herpes simplex was isolated by injecting the material from a vesicle into a rabbit's cornea. Hemolytic *Streptococcus albus* isolated from a vesicle was considered a secondary invader. A comprehensive review of the literature of Kaposi's varicelliform eruption and a discussion of the disease are included. E. H. W.

Specificity of Eczematous Hypersensitivity to P-Amino-benzoic Acid Butylester ("Butesin"). Laden, E. L., and Rubin, L.: Proc. Soc. Exper. Biol. & Med. **66**: 451, 1947.

A patient with contact dermatitis resulting from the application of butesin picrate ointment was studied. Patch tests performed with related compounds yielded positive reactions only to the alkyl esters of p-amino-benzoic acid. The positive reactors were tested quantitatively to determine the lowest concentrations at which reactions could just be elicited. Increased sensitivity was associated with lengthening of the side chain, reaching a maximum with the propyl ester. Decreased sensitivity occurred with further lengthening of the side chain. Tests with the isocompounds caused less reaction than the isomer n-compounds. The sensitivity pattern described demonstrates a rather narrow range within a well defined chemical configuration, with the maximum sensitivity found not with the sensitizing agent, but rather with one of the related homologues.

B. SIEGEL.

Feverfew Dermatitis. Daniels, A. K.: Brit. J. Dermat. **59**: 340, 1947.

A 39-year-old farmer developed severe eczematous dermatitis of the exposed skin surfaces after harvesting in a flax field. Patch tests with flax were negative, but tests with threshing dust showed strongly positive reactions. Testing with the components of the threshing dust indicated extreme sensitivity to "feverfew," a plant which grows wild throughout Britain in waste ground and hedgerows. It has a branched stem with flowers that resemble a daisy. It grows about two feet high and flowers from July to September. C.

The Production of Dermatitis by Pyrethrum and Attempts to Produce a Non-Irritant Extract. Lord, K. A., and Johnson, C. G.: Brit. J. Dermat. **59**: 367, 1947.

Ten per cent of sixty-two male subjects and twenty-six per cent of twenty-seven female subjects were sensitized to a dermatitis-producing, mosquito-repellent ointment by the daily application of the ointment behind the right ear for a period of five weeks. Application of the cream to the arm of the previously sensitized subjects was followed within two or three days by a local reaction similar to the reaction observed behind the ear, indicating that sensitization was general.

Three of the sensitized men were tested with the colorless concentrate (40 per cent Pyrethrum) and with the tragacanth base. They showed positive reactions within twenty-four hours to the Pyrethrum extract but not to the tragacanth base.

Petroleum ether extracts of Pyrethrum flowers were tested on subjects who had previously been sensitized to the commercial concentrate (40 per cent Pyrethrum). No correlation was found to exist between the Pyrethrum content of the various preparations and the degree of skin irritation observed. This suggests that the dermatitis factor may not be associated with the Pyrethrum content. C.

Otorhinology and Ophthalmology

Immunological Studies With Common Cold Infection. Pollard, M., and Caplovitz, C. D.: Am. J. Hyg. **47**: 106, 1948.

Bacteria-free nasal washings from acute cases of common cold infection were instilled in human subjects to determine the duration of immunity induced

by infection and the effect of chick embryo passage on the virulence of the virus. Six of eight subjects were immune to an inoculation of cold virus eleven to thirty days after the onset of an experimentally induced cold. The two remaining individuals developed mild colds following experimental inoculations. Three strains of virus were passed through several chick embryos. Two strains were attenuated greatly by three or less passages, and one, the Spill strain, actively induced colds after twelve passages although the virus from the later passages of this series caused relatively mild symptoms. Ten human subjects who were given two weekly subcutaneous injections of the chick embryo-propagated Spill strain were fully protected from a virulent cold virus while nonimmunized controls developed severe colds.

It is suggested that immunity to the common cold may depend in part on some degree of systemic infection with the virus. K.

Accidental Poisoning With Naphazoline (Privine) Hydrochloride. Hainsworth, W. C.: Am. J. Dis. Child. **75**: 76, 1948.

A 22-month-old child swallowed 3 or 4 ml. of 0.1 per cent Privine. Toxic symptoms ensued within fifteen minutes consisting of excessive thirst, tachycardia of 130 to 140 per minute, and lethargy with irritability on being roused. The pulse rate was 60 to 80 per minute at the end of one hour. In two hours the patient had irregular gasping respirations and became unconscious. At the time of hospitalization the skin was cold and clammy, the blood pressure was 170 systolic and 150 diastolic, the temperature was 97°, and the pulse rate was 60 beats a minute. Caffeine and oxygen were given to combat the central nervous system depression. The blood pressure returned to normal in nine hours and all symptoms subsided within fifteen hours. There were no sequelae. K.

Miscellaneous Allergies

Passive Cellular Transfer of the Tuberculin Type of Hypersensitivity. Stavitsky, A. B.: Proc. Soc. Exper. Biol. & Med. **67**: 225, 1948.

White albino guinea pigs, actively sensitized with killed tubercle bacilli and adjuvants, were injected intraperitoneally with mineral oil to evoke a peritoneal exudate, and sacrificed forty-eight hours later. Normal unsensitized guinea pigs were then inoculated intraperitoneally with the washed peritoneal cells, or with splenic cells, lymph node cells, whole defibrinated blood, citrated blood, or serum from the sensitized animals. At twenty-four and forty-eight hours after the transfer, the recipient animals were injected intracutaneously with 0.1 ml. of deglycerinated broth as a control. When peritoneal, splenic, and lymph node cells were used, the tuberculin sensitivity was passively transferred in almost all instances. At the test site a positive tuberculin reaction of the delayed type usually appeared in about twenty-four hours, reached its height in forty-eight to seventy-two hours, and lasted about four or five days. Tuberculin sensitivity was passively transferred by defibrinated or citrated blood in two of six trials, but was not transferred when serum was used. This suggested the importance of white blood cells in the transfer phenomenon. Controls with peritoneal and splenic cells from normal animals gave negative results. The positive results with the lymph node cells, containing 95 per cent lymphocytes, suggests the importance of this type of cell in the transfer of the tuberculin type of hypersensitivity. B. SIEGEL.

Periarteritis Nodosa-like Lesions in Tuberculous Meningitis. Bohrod, M. G.: N. Y. State J. Med. **48**: 275, 1948.

A case of tuberculous meningitis was observed in which there were an unusual number of remarkably well defined vascular lesions, histologically identical with those seen in periarteritis nodosa. The vascular lesions were limited, however, to the meninges. It is suggested that this may represent an instance of the allergic nature of periarteritis nodosa lesions in which the allergen was tuberculo-protein and in which the meningeal blood vessels were hypersensitive to this allergen. The apparent absence of tubercle bacilli in the vascular lesions may lend some support to this view. C.

Tests of Possible Antagonism of Gold for Histamine Toxicity and Certain Allergic Reactions. Kuzell, E. C., and Dreisbach, R. H.: Proc. Soc. Exper. Biol. & Med. **67**: 157, 1948.

In view of the beneficial effects which are attributed to gold salts in rheumatoid arthritis and because of the belief that there is an allergic factor in this disease, experiments were performed to study the effect of the gold ion on experimental allergic reactions. It was found that gold sodium thiosulfate failed to protect guinea pigs against anaphylactic or histamine shock and did not prevent the development of the characteristic wheal in the Arthus phenomenon in rabbits. It was concluded that the favorable action of the gold ion in rheumatoid arthritis is not based on the inhibition of allergic responses. B. SIEGEL.

Observation on Acute Allergic Gastritis. Afendoulis, T. C.: Am. J. Digest. Dis. **15**: 90, 1948.

Three cases of gastritis of allergic etiology are presented. Urticaria and gastric symptoms followed the ingestion of antipyrine, curdled milk, and cheese. The diagnosis of gastritis was made by gastroscopy. The changes in the gastric mucous membranes were similar to those found in nonallergic acute gastritis except that the reactions were more intense and more sudden in onset. The reaction is attributed to products of incomplete breakdown of proteins, particularly to histamine or histamine-like substances, acting directly upon the mucous membrane. Repeated attacks may lead to chronic gastric atrophy with anacidity. F.

Treatment of the Migraine Attack. Friedman, A. P., and Brenner, C.: Am. Pract. **2**: 467, 1948.

Ninety-four patients suffering from typical attacks of migraine were treated with the various types of medication. The most satisfactory results were obtained with ergotamine tartrate and its derivatives which afforded relief in 53 per cent of the cases and no benefit in 27 per cent. The vasodilators afforded relief in 13 per cent of the cases and no benefit in 65 per cent while the analgesics were effective in 21 per cent and failed in 56 per cent. Combinations of ergotamine tartrate with caffeine (for oral administration) or with atropine (as rectal inserts) proved more effective than either ergotamine tartrate alone or dihydroergotamine methanesulphonate. In using ergotamine tartrate or its derivatives, it is important that adequate dosage be administered early in an attack to obtain the best results. Preliminary studies with dihydroergocornine were disappointing. F.

Fatal Anaphylaxis Following Typhus Vaccine Injection. Walker, R. H.: U. S. Nav. M. Bull. **48**: 303, 1948.

A 20-year-old white sailor while on board ship was given a subcutaneous injection of typhus vaccine. Twenty-six minutes later he was found dead. The patient was known to be egg-sensitive. Autopsy findings revealed only pulmonary congestion. F.

The Diagnosis of Histoplasmosis in Ulcerative Disease of the Mouth and Pharynx. Weed, L. A., and Parkhill, E. M.: Am. J. Clin. Path. **18**: 130, 1948.

Of seventy-three cases of histoplasmosis recorded in the literature, twenty-four complained of oral lesions. Four additional cases are added. In three, no note is made as to whether they showed skin sensitivity to histoplasmin. In the fourth patient, a 77-year-old man with oral symptoms of two months' duration and a marked loss of weight, the histoplasmin skin test was negative. K.

Unsuccessful Attempts to Produce Periarteritis Nodosa Experimentally. Alston, J. M., Cheng, K. K., and Short, R. H. D.: J. Path. & Bact.: **59**: 490, 1947.

An attempt was made to produce periarteritis nodosa in rabbits by repeated injections of horse serum after the method of Rich and Gregory. Twenty-five animals were treated over a period of thirty-three days. The rabbits were sacrificed twenty-eight to thirty-five days after the initial injection. The organs of all the animals were examined grossly; microscopic examinations of the tissues of fifteen animals were also made. No lesions resembling periarteritis nodosa were found.

A second series of ten rabbits received a more intensive course of injections of horse serum over a period of thirty-three days. All were sacrificed two days later. Both gross and microscopic examinations failed to reveal any lesions suggestive of lesions of periarteritis nodosa. J. SHERMAN.

Anaphylaxis

Effect of Passive Sensitization and Anaphylactic Shock on Rabbit Bone Marrow. Good, R. A.: Proc. Soc. Exper. Biol. & Med. **67**: 203, 1948.

Young adult albino rabbits were passively sensitized with anti-egg white rabbit serum. Twenty-four hours later, anaphylactic shock was produced by the intravenous injection of egg white. Bone marrow biopsies were performed before and eighteen hours after sensitization, and eight, twenty-four, and ninety-six hours after anaphylactic shock. Differential counts on these bone marrow specimens were compared with corresponding counts from actively sensitized rabbits. It was found that in the actively sensitized animals the plasma cellular reticulum cell content rose before shock and the plasma cell content rose after anaphylactic shock. These increases were not noted in the passively sensitized animals. It is therefore concluded that the bone marrow plasmacytosis seen in active sensitization and shock is produced by factors other than the reticular reaction secondary either to the presence of altered globulin in the form of antibody protein or factors related to anaphylactic shock, per se. B. SIEGEL.

Toxicity of Equine Serum Treated by Alkali. Zia, S. H.: Proc. Soc. Exper. Biol. & Med. **67**: 189, 1948.

Normal horse serum was treated with 0.25 normal solution of sodium hydroxide for thirty days and kept at 37°. When rabbits were immunized with the treated serum, precipitins were not produced against either normal or treated sera and only occasional complement fixation reactions were obtained with both sera. Only half of these immunized animals showed positive skin reactions to normal serum. About half of the sensitized guinea pigs were mildly shocked with normal or alkali-treated serum. Normal rabbits tolerated intravenous injections of treated serum, while about half of the sensitized rabbits showed only a slight elevation of body temperature when similarly treated. Twenty-three of twenty-six normal white mice survived an intracutaneous injection of treated serum. One of three normal guinea pigs died when given less than 100 mg. of treated serum protein intracardially, but 120 to 240 mg. of serum protein proved lethal for all guinea pigs. It was concluded that equine serum is rendered practically nonantigenic when treated with alkali. The treated serum was definitely toxic for guinea pigs and practically nontoxic for rabbits and white mice. B. SIEGEL.

Histamine Shock in Mice Sensitized With Hemophilus Pertussis Vaccine. Parfentjev, A., and Goodline, M. A.: J. Pharmacol. & Exper. Therap. **92**: 411, 1948.

Mice injected with from five to seventy-five billion *Hemophilus pertussis* bacteria in vaccine form developed hypersensitivity to histamine by the fifth day after the injection. The sensitivity persisted at a high level for eleven or twelve days. The sensitized mice were about as reactive to 2 mg. histamine diphosphate as normal mice were to 50 milligrams. Larger doses of vaccine produced greater histamine sensitivity. Typhoid vaccine or normal horse serum failed to sensitize to histamine. K.

Pharmacology and Physiology

The Biological Assay of Histamine and Diphenhydramine Hydrochloride (Benadryl Hydrochloride). Chen, G., Ensor, C. R., and Clarke, I. G.: J. Pharmacol. & Exper. Therap. **92**: 90, 1948.

Using guinea pig ileum as an indicator, studies were made on the effects of variations in the doses of histamine and of Benadryl in combination with the smallest effective doses of histamine. The height of the contractions were expressed in terms of percentage of the maximal contraction. Statistical analysis of the relationships between dose and response, expressed in terms of probits and log doses, indicated a linear relationship. It is important that the assay of an unknown sample of histamine or Benadryl be compared with a standard on the same ileum. There is a significant difference on the regression coefficients to histamine with and without Benadryl. Comparison of the 50 per cent effective concentrations of Benadryl and histamine shows that the action of histamine may be antagonized by 0.1 equivalents of Benadryl. These observations support the reports of others that the antagonism of histamine by Benadryl is not due to simple chemical union between the two substances. It is suggested that Benadryl may act on certain enzyme systems which are affected by histamine. K.

Pharmacological Properties of a New Antihistaminic, 2-Methyl-9-Phenyl-2,3,4, 9-Tetrahydro-1-Pyridindene (Thephorin) and Derivatives. Lehmann, G.: J. Pharmacol. & Exper. Therap. **92**: 249, 1948.

Thephorin which is chemically unrelated to either Benadryl or Pyribenzamine was found to compare favorably with these drugs in its ability to counteract the effects of histamine administered to guinea pigs as a spray or intracardially. Studies on the isolated guinea pig ileum confirmed this antihistaminic effect. Anaphylactic shock was also counteracted, but less effectively than histamine shock. The drug is a more potent local anesthetic than procaine and its acute toxicity is comparable to that of Benadryl. Fatal doses in mice, guinea pigs, rabbits, and dogs cause convulsions followed by paralysis and respiratory depression. Chronic toxicity studies conducted on rabbits and dogs over a period of eight months failed to reveal pathologic changes attributable to Thephorin. K.

Side Reactions to Pyribenzamine Medication. Brown, S. I.: Proc. Soc. Exper. Biol. & Med. **67**: 373, 1948.

During the twenty-four-hour period after they received injections of typhoid vaccine, 144 subjects were given either 250 or 500 mg. of Pyribenzamine or placebos. It was found that the incidence of drowsiness, nausea, dizziness, and insomnia was greatest in the group receiving the larger dose of Pyribenzamine, less in the group receiving the smaller dose, and least in the control group. Headache was more frequent in the control group than in the other two groups. Nervousness and dryness of the mouth occurred as frequently in the smaller dose group as in the control group, but increased in frequency when the dose of Pyribenzamine was doubled. The importance of using control studies in evaluating a new drug was stressed. B, SIEGEL.

Untoward Side Effect Following Benadryl Administration. Swartz, H.: N. Y. State J. Med. **48**: 88, 1948.

Symptoms of acute labyrinthitis developed in a 32-year-old atopic patient on the sixth day following symptomatic treatment of hay fever with Benadryl. Symptoms regressed after the withdrawal of the drug and reappeared on two other occasions when Benadryl was administered orally in either the elixir or "Kapseal" form. C.

Miscellaneous

Immunity to Diphtheria Induced by a Booster Dose of Diphtheria Toxoid Purified by Absorption and Elution. Peshkin, M. M., and Rapaport, H. G.: Ann. Allergy **5**: 503, 1947.

Purified diphtheria toxoid was prepared from absorbed toxin by detoxification with formaldehyde, dialysis and absorption with calcium phosphate and eluted toxoid was prepared from this product. Fifty-five allergic children, all of whom had been previously immunized with combined alum-precipitated diphtheria and tetanus toxoids, received 0.5 or 1.0 c.c. booster doses of purified diphtheria toxoids. All of these patients had had asthma or hay fever or both. Both the calcium phosphated and eluted toxoids possessed marked antigenic potency of equal degree, the maximum antitoxin response occurring within two months. The responses to booster doses of 0.5 and 1.0 c.c. were approximately the same. Of thirty children injected with calcium phosphated toxin, sixteen developed severe and eleven, moderate local reactions. Six of these children

had a febrile response. Among thirteen patients injected with similar doses of the eluted toxin, there were four with severe and four with moderate local reactions. A febrile response occurred in only one of these patients. Comparative intradermal tests were made with a 1:100 dilution of crude yellow toxoid and eluted calcium phosphated toxoid in 113 allergic children ranging in age from 8 to 15 years. All of these children had been previously immunized in early childhood. Delayed reactions to yellow toxoid occurred in twelve children of whom four also reacted to eluted toxoid. Ten other children reacted to both toxoids but the response to the eluted product was definitely smaller. Eluted calcium phosphated diphtherial toxoid is recommended since it diminishes the incidence of local, febrile, or systemic reactions when used in allergic children. E. H. W.

Immunization of Adults With Diphtheria Toxoid. I. Immunological Properties of Formalinized Diphtheria Protein Fractions From Culture Filtrates. Lawrence, H. S., and Pappenheimer, A. M.: Am. J. Hyg. **47**: 226, 1948.

An attempt was made to determine which constituents of formalinized culture filtrates are responsible for the severe reactions encountered in adults immunized with standard diphtheria toxoids. Reactions to broth culture media were eliminated by using a peptone-free medium. A formalinized mixture of atoxic diphtherial proteins ("P-fraction") containing less than 0.23 per cent toxoid and a purified diphtheria toxoid containing little P-fraction were used to sensitize rabbits and guinea pigs. Precipitin tests and anaphylaxis experiments showed minimal cross-reactivity between these two fractions, whereas crude toxoid reacted almost maximally with both preparations. K.

Immunization of Adults With Diphtheria Toxoid. II. An Analysis of the Pseudoreactions to the Shick Test. Pappenheimer, A. M., and Lawrence, H. S.: Am. J. Hyg. **47**: 233, 1947.

The reactions of 186 young adults to the Shick test were studied using purified diphtheria toxoid, a toxoid-free atoxic diphtheria protein mixture ("P-fraction,") and crude toxoid preparations. Both Shick-positive and Shick-negative individuals may be predominantly sensitive to "P-fraction" or pure toxoid, to neither, or to both. Most Schick-positive individuals showed some sensitivity to P-fraction and were insensitive to the toxoid itself. Most Shick-negative pseudoreactors were exquisitely sensitive to both P-fraction and to toxoid. The Shick-negative group reacted most severely to the toxoid itself. All cases with delayed cutaneous reactions to purified toxoid showed circulating antitoxin in the blood prior to testing. The severity of allergic reactions to toxoid seems to vary roughly with the titre of circulating antitoxin, the more severe reactions tend to occur in those with higher antitoxin levels. However, high antitoxin levels are not infrequently observed in individuals having no demonstrable cutaneous sensitivity. K.

Immunization of Adults With Diphtheria Toxoid. III. Purified Toxoid as an Immunizing Agent. Pappenheimer, A. M., and Lawrence, H. S.: Am. J. Hyg. **47**: 241, 1948.

Since most previously immunized Shick-positive adults are sensitive to toxoid-free atoxic diphtherial proteins (P-fraction) rather than to toxoid itself, immunization of these persons with purified toxoid should be feasible with a minimum of undesirable reactions. On the other hand, Shick-negative individuals would be expected to show a high proportion of severe general reactions to

purified toxoid. Fifty-seven young Shick-positive adults were immunized with purified toxoid. No severe local or general reactions were encountered and the circulating antitoxin response was satisfactory. Of three Shick-positive individuals found to be sensitive to purified toxoid, all produced between one and twenty units of antitoxin per milliliter within three weeks of the intracutaneous injection of only 0.002 ml. toxoid, an excellent anamnestic response. Thirty nurses were Shick tested with purified toxoid in regular Shick test strength and with purified toxoid ten times more concentrated. Ten were found to be Shick-positive. Retesting one month later showed only four of the original ten still positive. These four were then immunized with no untoward reactions. K.

Observations on the Safety of Multiple Antigen Preparations. Volk, V. K.: Am. J. Hyg. **47**: 53, 1948.

Injections were carried out on groups of children and adults totalling 2,791 individuals. From one to five of the following antigens were injected: fluid diphtheria toxoid, pertussis vaccine, scarlet fever toxin, half-strength tetanus toxoid, alum-precipitated tetanus toxoid, typhoid-paratyphoid A and B, typhoid vaccine, and streptococcus vaccine. Three doses were given and the reactions to each carefully noted. When 0.5 ml. was administered, general reactions were negligible although some occurred in the group given 1.0 ml. of the same preparation. Intramuscular injection resulted in fewer reactions and much less "antigenic cyst" formation than when the subcutaneous route was utilized. Adults were more prone to reactions than children, and the third injection of antigen in an individual was apt to be more troublesome than the first two. The inclusion of typhoid vaccine in the mixture increased the reactions thereto. Reactions following a mixture of alum-precipitated diphtheria toxoid, pertussis vaccine, and scarlet fever toxin were only slightly more severe than those following diphtheria toxoid alone.

While five-antigen preparations containing typhoid vaccine produce more reaction than three-antigen or single antigen preparations, the more inclusive vaccines are safe for use in areas where typhoid fever is prevalent. "Over 90% of all general reactions were mild and only very few individuals in the entire group could be considered as having had moderate or severe general reactions." K.

An Improved Colorimetric Method for the Estimation of Histamine. Rosenthal, S. M., and Tabor, H.: J. Pharmacol. & Exper. Therap. **92**: 425, 1948.

Previous colorimetric methods for the assay of histamine have been unsatisfactory because of instability of colors, lack of specificity, and interference by numerous substances in biological extracts. A new colorimetric technique for the determination of free and conjugated histamine in body tissues and fluids is described in detail. The sensitivity of this method is about 0.5 micrograms. K.

Attempts to Inhibit Rh Antibody Production in Rabbits. Use of Ethylene Disulphonate, Sodium Salicylate, Pyribenzamine, and A and B Specific Blood Substances. Scherer, W. F.: Am. J. M. Sc. **215**: 33, 1948.

In an effort to inhibit or reduce Rh antibody production, various substances were administered subcutaneously to rabbits who were at the same time receiving injections of Macacus rhesus cells. An average of 85 per cent of the rabbits in the series developed agglutinating and conglutinating Rh antibodies. No

reduction or inhibition of Rh antibodies was effected by the administration of Ethylene Disulphonate, Sodium Salicylate, Pyribenzamine, and A and B Specific Blood Substances. F.

Reactions to Concentrated Influenza Virus Vaccine. Salk, J. E.: J. Immunol. **58**: 369, 1948.

The degree of delayed febrile reaction and the immunologic response following the injection of various doses and types of influenza virus were investigated. It was found that the incidence of influenza-like symptoms varied with the quantity of biologically active virus administered rather than with the protein nitrogen content of the vaccine. Purification of the virus by centrifugation did not diminish the incidence of these reactions. On the basis of serologic studies, it was found that the quantity of virus injected could be varied within relatively broad limits without causing a significant variation in the antibody response. However, only a small increase in quantity of active virus injected was necessary to cause an appreciable increase in the incidence of systemic reactions. It was therefore suggested that the dose of virus for vaccination could be safely adjusted to sub-reactive levels without sacrificing its immunizing effect. It was also suggested that the various strains of virus have different capacities for producing systemic reactions and have different antigenic qualities. It remains questionable whether the systemic reaction represents a true toxic effect of the virus or a phenomenon due to previous sensitization to the virus.
B. SIEGEL.

Immunologic Reactions Following the Intradermal Inoculation of Influenza A and B Vaccine. Weller, T. H., Cheever, F. S., and Enders, J. F.: Proc. Soc. Exper. Biol. & Med. **67**: 96, 1948.

Four hundred and forty-nine hospital employees were injected intracutaneously with 0.1 ml. of a 1:5 dilution in 0.85 per cent salt solution of mixed A and B Influenza vaccine. Immediate and delayed local erythematous reactions exceeding 10 mm. in diameter were noted in about 85 per cent of the cases. Systemic reactions were reported in 16.7 per cent of the subjects. Blood specimens were drawn before and three weeks after vaccination from thirty-nine individuals who had not had an upper respiratory infection in the interim. Following vaccination, the geometric mean of the antihemagglutinin titer rose 2.9 times for Influenza B and 3.6 times for Influenza A. The latter rise could not be attributed conclusively to the inoculation since an epidemic caused by an atypical Influenza A virus was current at the time of the study. There was no correlation between the intensity of the local reaction and the antibody response. The antibody titer increase was most marked when the initial titer was low. The antihemagglutinin levels obtained with the intracutaneous technic were only slightly lower than the levels reported with the standard subcutaneous vaccination. The prophylactic value of the intracutaneous vaccination was not demonstrated in this study. In the presence of an Influenza A epidemic in the community, the upper respiratory disease rate during the two-month period of observation was approximately the same in the vaccinated group and in the control unvaccinated group working in the same hospital. B. SIEGEL.

Allergy Abstracts

Asthma and Hay Fever

Management of Bronchial Asthma. The Use of 1-(3′,4′-Dihydroxyphenyl) -2-isoproprylaminoethanol. Segal, M. D., and Beakey, J. E.: Ann. Allergy **5**: 317, 1947.

The therapeutic efficacy of Isuprel, 1-(3′,4′-Dihydroxyphenyl) -2-isoproprylaminoethanol, was studied in 122 asthmatic patients. The series included ambulatory and hospitalized patients of the intrinsic and extrinsic types. When Isuprel, in concentrations of 1:100 or 1:200, was administered as an aerosol, it was found that the greater the bronchospasm, the greater was the increase in vital capacity as a result of treatment. Improvement in vital capacity was also noted in patients with asthmatic cough, although no clinical evidence of bronchospasm was present. Patients with severe asthma received 1 ml. of a 1:100 dilution of aerosolized Isuprel every three hours. Under this regime, twenty-seven patients during thirty-seven admissions were markedly improved. Administered subcutaneously in dosage varying from 0.25 ml. to 0.75 ml. of a 1:1000 dilution, Isuprel markedly increased the vital capacity of eleven epinephrine-fast patients. The effects were not long-lasting and treatment had to be repeated every three or four hours. Subcutaneously administered, Isuprel was effective in breaking the cycle of status asthmaticus. Isuprel administered orally was ineffective in the management of acute asthma. The fluctuations in systolic and diastolic blood pressure readings in inspiration and expiration were abolished or markedly decreased following treatment with Isuprel. Side reactions consisted of jitters and palpitation and were more severe when the drug was administered by the subcutaneous route. Nausea, vomiting, and dizziness were also encountered. No refractoriness to Isuprel was observed. E. H. W.

Chemical Investigations of Giant Ragweed Pollen. Part I. Stone, G., Harkavy, J., and Brooks, G.: Ann. Allergy **5**: 546, 1947.

The dialysate of a defatted aqueous solution of giant ragweed was subjected to a systematic elimination of various protein components by precipitation with easily removable precipitants. The allergenic potency of the various extracts and fractions was compared to that of a standard ragweed extract containing 0.01 mg. nitrogen per milliliter by intracutaneous testing of ragweed-sensitive patients. The dialysate of the defatted ragweed extract was about one-half as active as the original solution. Heating the dialysate to 100° C. for one-half hour, buffering it at pH 4 or 8, or shaking it with an equal volume of a 1:1 mixture of butyl alcohol and chloroform, failed to alter its allergenic potency. Treatment with 5 per cent trichloracetic acid and subsequently with saturated picric acid did not precipitate the active principle or alter the skin reactivity of the extract. The active principle was precipitated by phosphotungstic acid and subsequently recovered from the precipitate. The purified fraction yielded positive ninhydrin, Biuret, and Molisch tests. The active principle in the dialysate was a comparatively low molecular weight peptide or carbohydrate, a mixture of the two, or a nitrogen containing carbohydrate. E. H. W.

Allergenic (Skin-Test) Activity of Low Ragweed Pollen After Irradiation of Extract With Ultraviolet Light. Brown, F., and Loveless, M. H.: Ann. Allergy **6**: 7, 1948.

The allergenic activity of low ragweed extract exposed to ultraviolet irradiation was investigated. One portion of low ragweed extract was subjected to irradiation at six inches through a glass barrier for one hour and another portion was similarly treated without the glass barrier for thirty minutes. Both were compared with untreated extract on ragweed-sensitive patients. The concentrations of extract which elicited threshold responses were compared. Cross-neutralization studies were also made. It was found that irradiation of low ragweed extract with the doses of ultraviolet light employed had no effect on the cutaneous reactivity of the extract. E. H. W.

Dermatology

Pruritus Vulvae From Rubber Due to Allergic Sensitivity to Alkali. Clarke, G. H. V.: Brit. J. Dermat. **60**: 57, 1948.

Pruritus vulvae in a 27-year-old woman was traced to the presence of free alkali from potassium oleate used as a stabilizer in the manufacture of rubber condoms. Results of identical patch tests made on the back, forearms, and hands indicated that the forearm is slightly less sensitive and that the hands are considerably less sensitive than the back. C.

Severe Allergic Sensitization to an Estrogenic Cream. Cole, H. N., Jr., Marmelzat, W. L., and Walker, A. E.: Ohio State M. J. **44**: 472, 1948.

A patient suffering from giant urticaria of nine weeks' duration was hospitalized and failed to respond to the usual therapy consisting of elimination diets, avoidance of drugs, and the administration of ephedrine and antihistaminics. On the eighth day in the hospital she had a severe flare-up of her symptoms. Investigation revealed that the exacerbation had followed the use of an estrogenic cream. Patch tests with this cream produced an area of giant urticaria. The patient subsequently was able to associate the exacerbations of her urticaria with the use of the estrogenic cream. F.

Allergic Dermatitis From Vaginal Absorption of Sensitizers (Floraquin and Verazeptol). Swinny, B.: Ann. Allergy **5**: 490, 1947.

Drug sensitization induced by vaginal absorption of the allergens occurred in two patients. A pruritic maculopapular rash of the scalp and neck followed the use of Floraquin suppositories for the treatment of trichomonas vaginitis in one patient. Patch testing with Floraquin duplicated the original lesions. A second patient, known to be sensitive to ammoniated mercury, developed a maculopapular eruption following the use of Verazeptol douche powder. Patch tests with Verazeptol 10 per cent and zinc sulfate 5 per cent were positive. Negative reactions were obtained on testing with other ingredients of the douche powder. The vaginal mucosa was normal in both patients. E. H. W.

Treatment of Allergic and Some Other Dermatoses With Theophorin. A Preliminary Report. Kesten, B. M., and Sheard, C.: J. Invest. Dermat. **9**: 65, 1947.

Theophorin (2-methyl-9 phenyltetrahydro-1 pyridindene acid tartrate) relieved the pruritus of two patients with serum sickness, of three with dermo-

graphism, and of thirty-six with urticaria of various types. The pruritus of erythema multiforme, papular urticaria, neurodermatitis, pruritus ani, and allergic eczema was also alleviated, but the itching of Hodgkin's disease or eosinophilic disease of the skin was unaffected. The pruritus of dermographism as well as of specific or histamine wheals was prevented by prior administration of the drug. The whealing in experimental or clinical urticarial lesions was not affected by Theophorin. Side reactions necessitated discontinuance of the drug in one-fourth of the patients treated. Nausea, anorexia, headache, drowsiness, palpitation, restlessness, depression, vomiting, indigestion, itching, and dizziness were the side reactions to Theophorin most frequently observed.

E. H. WALZER.

Sensitivity to Burnt Coal Gas. Mumford, P. B., and Auckland, G.: Brit. J. Dermat. **59**: 169, 1947.

Acute dermatitis of the face and neck in a nonatopic woman followed exposure to burnt coal gas. In an effort to determine the responsible irritant patch tests were performed with the various constituents of burnt coal gas and exposure tests were made to the same materials. A positive patch test was obtained with 1 per cent formaldehyde, indicating that the minute traces of aldehydes produced by burnt coal gas were responsible for the rash. Exposure to unburnt coal gas did not produce the dermatitis. C.

Reactions of the Vulva to Systemic Diseases. Parks, J., and Martin, S.: Am. J. Obst. & Gynec. **55**: 117, 1948.

The vulva often shows nonvenereal lesions which may be manifestations of systemic diseases, such as blood dyscrasia, uremia, diabetes mellitus, avitaminosis, or allergy. Allergic dermatitis of the skin of the vulva may result from drugs, soaps, and clothing. Common offenders are phenolphthalein, rectal ointments, and phenol-containing douching materials. Underclothing made of poorly processed rayon and containing incompletely fixed dyes, formaldehyde preparations, synthetic resins, and sulfonated oils, used to process rayon may act as sensitizing agents. Edema and itching of the labia occur first, followed by secondary trauma due to scratching. A careful history is essential in determining the offending agent. Patch testing is usually unsatisfactory. Two illustrative case histories are presented. J. SHERMAN.

The Allergen of Human Dander Present in Skin of the General Body Surface. Simon, F. A.: J. Invest. Dermat. **9**: 329, 1947.

Human body and scalp dander extracts were prepared from material obtained by expressing the fluid from ether-saturated cotton pledgets after they had been vigorously rubbed over the skin of the thighs and the scalp of a normal adult male. The scalp dander extract, being more active allergenically and more irritating, was diluted until it produced intracutaneous test reactions in dander-sensitive patients equal to those produced by the injection of body dander extract. A control extract was prepared from the absorbent cotton plus lint scraped off the man's trousers. Intracutaneous tests with these extracts on normal individuals gave negative reactions. Immediate reactions were obtained when the body and scalp dander extracts were injected intracutaneously in five dander-sensitive patients. Intracutaneous testing with the control extract gave negative reactions in four patients and a questionable reaction in one. Passive transfer tests with sera from two dander-sensitive patients were positive with these extracts. Antibody neutralization studies revealed that scalp dander

neutralized reagins for body dander and vice versa. It was thus concluded that the allergen in both extracts was identical.

Scalp and body dander extracts were similarly prepared from the skin of a 14-year-old girl with atopic dermatitis. Intracutaneous tests with these and control extracts gave negative reactions on normal individuals, but large immediate reactions on the patient. Using the patient's serum, the sensitivity to both extracts was transferred successfully. It was thus shown that patients may be allergic, not only to a substance in the skin of some other person, but also to this substance in their own skins. B. SIEGEL.

Delayed Reactions to Penicillin in Beeswax and Peanut Oil (P.O.B.) in a Child. Mandel, E. E., Basch, F. P., and Greengard, J.: Arch. Pediat. **65**: 119, 1948.

A 3-year-old child suffering from an upper respiratory infection was given three daily intragluteal injections of calcium penicillin in beeswax-peanut oil. Moderate swelling, erythema, and induration developed about the sites of the injections. Twenty-one days following the last intramuscular injection, the child developed painful swelling of the cervical glands, moderate generalized lymphadenopathy and fever. Twenty-four hours later generalized pruritus appeared followed by an erythematous and morbilliform rash which was later modified by urticaria and angioneurotic edema. At this time an eosinophilia of 24 per cent was found. The urticaria continued intermittently and was accompanied by a fine scaling of the skin for several weeks. Patch and intradermal tests with the original P.O.B. material, amorphous penicillin, and beeswax and peanut oil without penicillin were all negative. A moderate erythema occurred at the site of a scratch test with P.O.B. F.

Reconstitution of the Dermal Barrier to Fluid Diffusion Following Administration of Hyaluronidase. Hechter, O.: Proc. Soc. Exper. Biol. & Med. **67**: 343, 1948.

Sites on the arms of adult human beings were injected intracutaneously with 0.2 ml. of varying concentrations of hyaluronidase solutions. Twenty-four and forty-eight hours after the enzyme injections, 0.2 ml. of an 0.85 per cent sodium chloride solution was injected intracutaneously in the previously treated sites and the time of wheal disappearance recorded. Using the time of wheal disappearance as a measure of the barrier efficiency of the dermal hyaluronic acid gel to fluid diffusion, the percentage restoration of dermal hyaluronic acid was calculated. It was found that at twenty-four hours the restoration of the dermal barrier was inversely related to the dose of enzyme, while at forty-eight hours the barrier was completely restored. B. SIEGEL.

Possible Eczematous Cross-Hypersensitivity Between Paraphenylenediamine and Azo-Dyes Certified for Use in Foods, Drugs and Cosmetics. Baer, R. L., Leider, M., and Mayer, R. L.: Proc. Soc. Exper. Biol. & Med. **67**: 489, 1948.

The subjects in these experiments were twenty-five patients with hypersensitivity to paraphenylenediamine and twenty-one control subjects with hypersensitivity to unrelated substances or with no hypersensitivity at all. Patch tests were made with ten azo-dyes certified for use in foods and drugs, with paraphenylenediamine, and with a sample of azo-dyed nylon stocking material. All dyes were used in 2 per cent concentration in white petrolatum. In the paraphenylenediamine-sensitive groups, four of the ten azo-dyes elicited nineteen 2+ or greater reactions in 250 tests. In the control group, four reactions of similar

intensity were obtained with three of the azo-dyes. Since the three latter dyes were among the four azo-dyes giving the strongest reactions in the paraphenylenediamine-sensitive group, they were considered as primary irritants in the concentrations used. However, since the reactions in the control group were fewer in number and less intense, and since one of the dyes which was not a primary irritant in the concentration used gave positive reactions only in the paraphenylenediamine-sensitive group, it was believed that the positive reactions were due to a cross sensitivity to compounds of quinone structure. The problem of sensitization is discussed in the light of the continual exposure of large portions of the population to many of the certified azo-dyes by contact, ingestion, and probably also by inhalation. B. B. SIEGEL.

The Mechanism of Adhesive Plaster Irritation. Peck, S. M., Rosenfeld, H., and Glick, A.: J. Invest. Dermat. **10**: 367, 1948.

Adhesive tapes produce three types of irritation. Type I is a relatively unimportant evanescent reaction, mostly erythema which is marked in hairy areas and is due to the mechanical trauma of removing the tape. Type II is a severe reaction due to specific sensitivity to one or more ingredients of the adhesive tape. It is relatively rare. Type III is the most common type of reaction and consists of erythema, edema, papules, and pruritus. Vesicles are rare. Sensitization is not the cause of this type of reaction and duration of contact with the skin is regarded as an important factor in its production.

A study of the mechanism of the third type of adhesive dermatitis was made by comparing the dermatitis producing effects of two varieties of adhesive tape. One contained zinc propionate and zinc caprylate and the other was ordinary hospital adhesive tape. The special adhesive tape produced no itching and no dermatitis when tested on 137 adults. Studies of the pH of normal skin revealed that the average pH was 5.2. The pH under the adhesive causing the greatest irritation rose to 6.3 at the end of seven days. At the end of fourteen days, it was 6.7. Under the adhesive containing the fatty acids, the pH was 5.7 at the end of seven days and 6.4 at the end of fourteen days. A decrease in bacterial flora was particularly striking under the adhesive containing the bacteriostatic and bacteriocidal fatty acid salts. Hence, fatty acid salts incorporated in adhesive plaster play an important role in preventing dermatitis by depressing the bacterial flora. Fatty acid salts failed to prevent dermatitis caused by specific sensitization. H.

Permanent Wave Process. Clinical Report With Special Reference to the Effect of Ammonium Thioglycolate on the Skin. Goldman, L., Mason, L., and McDaniel, W.: J. A. M. A. **137**: 355, 1948.

In the process of cold-waving hair, an alkaline reducing agent, usually thioglycolate, is used along with the following: a preliminary shampoo, a preliminary cleansing lotion, an oxidizing agent, a posttreatment shampoo, a wave-setting material and perfumes. The effect of the application of diluted and undiluted ammonium thioglycolate was investigated in 149 women with apparently normal skins and scalps. One drop of the undiluted material was applied with a glass rod and rubbed into the skin in the occipital region and on the forehead just below the hair line. This was called the "streaking test." Patch tests were also made on the arms of some of these subjects and read in forty-eight hours. Positive reactions were obtained in only two of the subjects tested by the streaking method with the undiluted material. Eleven of the eighty-three subjects patch-tested showed positive reactions. There was no correlation between the positive reactions from the streaking tests and those from the patch tests. The results suggest that ammonium thioglycolate is a mild primary irritant.

Twelve beauty parlor operators suffering from contact dermatitis of the hands showed negative reactions to patch tests with the cold wave material but tests with shampoos yielded some positive reactions. Hence, the majority of dermatitides related to the cold wave process are due to direct irritation and not to sensitization. The reactions on the hands of the operators are more frequent, severe, and extensive than those seen in patrons. F.

Studies on the Eczematous Sensitization. III. The Effect of the Engendering of an Eczematous Sensitization on the Threshold of Reaction to Primary Irritants. Haeberlin, J. B., Jr., Oliver, R. M., and Rostenberg, A., Jr.: J. Invest. Dermat. **10**: 27, 1948.

Dilutions of three primary irritants, hydrochloric acid, tincture of green soap, and croton oil, were so made that the weakest produced negative contact reactions and the strongest produced weakly positive contact reactions in the majority of the control subjects. Tuberculous subjects were patch tested with these solutions and the reactions were read after twenty-four hours. Following this, the test subjects were sensitized by dropping 0.03 ml. of a 30 per cent acetone solution of 2,4-dinitrochlorobenzene on the volar surface of the arm. After varying periods of time, patch tests with the primary irritants were repeated in sixteen subjects, eight of whom had been successfully sensitized with the 2,4-dinitrochlorobenzene. Results showed that the development of eczematous sensitization did not have any effect on the threshold of irritation to the primary irritants employed. The results may have been affected by the interference of the tuberculous infection on sensitization phenomena. B. B. SIEGEL.

Local Therapy With Pyribenzamine Hydrochloride. Sulzberger, M. B., Baer, R. L., and Levin, H. B.: J. Invest. Dermat. **10**: 41, 1948.

The therapeutic values of 2 per cent and 5 per cent Pyribenzamine hydrochloride creams applied locally three or four times daily were studied in ninety patients with a variety of dermatosis. Blank water miscible cream was used as a control. Included in the study were patients with disseminated neurodermatitis, allergic dermatitis of the contact type, circumscribed neurodermatitis, pruritus ani and vulvae, and a miscellaneous group. The only patients who appeared to be benefited by the Pyribenzamine cream were those with circumscribed neurodermatitis. In this group, 50 per cent of the patients were definitely improved by the therapy. In five subjects, the drug had to be discontinued because of untoward side effects. Two of these patients developed contact dermatitis with positive reactions to patch tests with the Pyribenzamine cream. It is concluded that the Pyribenzamine cream is of questionable value in dermatosis other than circumscribed neurodermatitis. B. B. SIEGEL.

Otorhinology and Ophthalmology

Atopic Cataract. Report of a Case With Tabulated Summary of Previously Reported Cases. Sack, S. Senior: Ann. Allergy **5**: 353, 1947.

The appearance of cataracts in young people suffering from disseminated neurodermatitis has been recognized since 1914. To date, sixty-one patients with cataract complicating neurodermatitis have been reported. Studies by American observers on thirty-three patients indicate that: (1) the family history for allergy is positive in most instances; (2) many of the patients have associated allergies; (3) most cataracts develop in the adolescent or early postadolescent stage; (4) blood eosinophile counts are usually 4 per cent or higher; (5) direct

skin tests with foods and inhalants are usually positive; (6) in three instances, when passive transfers were done, reagins were demonstrated in the blood serum. In the majority of patients the cataracts are bilateral.

Worthy of special note is the long interval that intervenes between the first appearance of the skin lesion and the development of the opacity, a period which averages about fifteen years. Also noteworthy is the speed with which the cataract matures once it starts, often within a few weeks. The changes in the lens are irreversible.

It is believed that the same factor which is responsible for the development of the neurodermatitis is also responsible for the formation of the cataract and that atopy is probably involved in both. The immediate mechanism whereby the cataract is produced is not known. The case presented is that of a girl, 17 years of age, in whom bilateral cataracts appeared after she had had a neurodermatitis for fifteen years. AUTHOR'S SUMMARY.

Miscellaneous Allergies

The Application of a Tissue Culture Technique in the Clinical Evaluation of Bacterial Hypersensitivity. Nantz, F. A., and Blatt, H.: Ann. Allergy **5**: 554, 1947.

A tissue culture technique was employed to demonstrate the presence of bacterial hypersensitivity. Antigens consisted of bacterial filtrates of twenty-four-hour broth cultures of various pathogens. The buffy coat was prepared from a plasma-free blood clot from which the red cells had been separated. The buffy coat was placed on a large rubber stopper and explants were prepared with a 1.5 mm. corneoscleral trephine. Each explant was placed on a glass with two drops of bacterial filtrate, one drop of fibrinogen, and one drop of thrombin. Upon coagulation of the explant, the cover glass was inverted over a hanging drop slide and incubated at 37° C. Normally, small wandering cells migrate so that within twelve hours they form a dense corona around the explant. Suppression of migration or the presence of necrosis was used as a measure of hypersensitivity. Slides were read in ten to forty-eight hours. Among fifty patients tested, forty showed no suppression when tested against *Streptococcus hemolyticus* group A, *Streptococcus viridans, Staphylococcus aureus* hemolyticus or anhemolyticus, and *Diplococcus pneumoniae,* in full strength. Six showed suppression in dilutions from 1:1000 to 1:10,000. Among these patients, two had asthma and one had recurrent bilateral keratitis. After specific desensitization, retesting may show a decrease in the hypersensitive state. E. H. W.

Periarteritis Nodosa With Recovery: Report of an Unusual Case Apparently Due to Sensitivity to Sulfadiazine. Goodman, M. J.: Ann. Int. Med. **28**: 181, 1948.

A 17-year-old student developed skin rash, nose bleeds, fever, and malaise suggestive of drug sensitivity. He had received several doses of sulfadiazine six weeks previously for a sore throat. The symptoms did not subside, but progressed rapidly to a fulminating, almost fatal illness. Hematuria, hypertension, generalized muscle tenderness, hemorrhagic phenomena involving skin and mucous membranes, and electrocardiographic evidence of myocardial damage suggested a widespread vascular lesion. Muscle biopsy established a diagnosis of periarteritis nodosa. At the height of illness, the patient was given full doses of sulfadiazine by error and in spite of repeated episodes of urticaria the drug was continued for five days. The patient began to improve rapidly after the drug was discontinued and made a complete recovery. H.

Histoplasmin and Tuberculin Sensitivity in Relation to Pulmonary Calcification Among University of Wisconsin Students. Dickie, H. A., and Clark, E. A.: Ann. Int. Med. **28**: 1087, 1948.

In a routine survey of 5,000 students by means of photofluorograms and tuberculin testing, 160 students with pulmonary calcifications were found to be tuberculin negative. In sixty-six of seventy-three cases, such calcifications were associated with histoplasmin sensitivity. Caution should be exercised in making a diagnosis of tuberculous infection solely on roentgenologic findings of pulmonary calcification or even of infiltrations since small pulmonary infiltrates roentgenologically indistinguishable from tuberculous lesions may be associated with histoplasmin sensitivity and not with tuberculin sensitivity. H.

Urticaria Caused by Heat, Exertion and Excitement. Report on Twenty-two Cases Among American Soldiers in Japan. Sigel, H.: Arch. Dermat. & Syph. **57**: 204, 1948.

Nineteen of the twenty-two cases of urticaria observed among American soldiers occurred during the cool autumn season within six months after their arrival in Japan from the tropical climate of the Philippine Islands or Florida. The other three patients had begun to have symptoms before they left the Philippine Islands. Generalized urticaria was readily produced by exertion, external heat, or excitement. Dermographism to a mild or modern degree was present in all cases. Ten patients had either a past personal or family history of allergy and one patient had a history of sensitivity to cold. Eosinophilia was absent in all cases. Intracutaneous tests with histamine showed no appreciable differences from a control group. Gastric acidity was not changed when urticaria was induced in eight patients by exposure to heat. Psychiatric examination in six patients revealed no abnormalities. Treatment on the whole was unsatisfactory in most cases. The milder cases seemed to be benefited by any form of treatment, while the more severe cases responded to none. Cooling agents were most effective in relieving symptoms. B. B. SIEGEL.

Anaphylaxis

Studies on the Sensitization of Animals With Simple Chemical Compounds. X. Antibodies Inducing Immediate-Type Skin Reactions. Chase, M. W.: J. Exper. Med. **86**: 489, 1947.

Guinea pigs were actively sensitized by repeated intracutaneous injections of oil solutions of adjuvants plus acyl chlorides, acid anhydrides, picryl chloride, 2:4 dinitrochlorobenzene, horse serum, or ragweed pollen. Local immediate and delayed reactions served as the index of sensitization. For passive local sensitization, 0.5 ml. of serum from sensitized guinea pigs was injected intracutaneously into other guinea pigs. After one or two days, the eliciting dose of antigen was administered either by injection into the sensitized site or at a distance. With citraconic anhydride, phthalyl chloride, phthalic anhydride, or o-chlorobenzoyl chloride, whealing and erythema appeared in most instances within three to forty-five minutes. The response to picryl chloride occurred in forty-five to two hundred minutes. The reaction to 2:4 dinitrochlorobenzene could be elicited only by the protein conjugate. Protein conjugates of the antigens were more effective in eliciting reactions at the passively sensitized sites.

Refractory periods immediately followed the sensitizing injection. The tested site was also refractory to a second antigen subsequently applied. The duration of passive sensitization was from five days to three or more weeks. The

sensitized sites reacted specifically to the homologous or a closely related antigen. The time required for a reaction to occur at the sensitized site was greater with substances of lesser chemical reactivity and more prompt reactions could be obtained with the protein conjugates of the simple chemical antigens.

Cross reactions which were weaker than homologous reactions occurred with closely related chemicals (phthalic anhydride, phthalyl chloride, citraconic anhydride). These cross reactions may be based on sensitization to even smaller molecular fragments than the phthalyl group. K.

A Note on Enzyme-Purified Antitoxin and Anaphylaxis in Guinea Pigs. Christensen, P. A., and Kerrich, J. E.: J. Immunol. **59**: 21, 1948.

Guinea pigs were actively sensitized by intra-abdominal injections of normal horse serum or with domestic or imported pepsin-purified diphtheria antitoxin. Twenty-one days later, the animals were challenged with varying doses of the various antigens. It was found that animals sensitized with normal horse serum were less easily shocked by pepsin-treated serum than by the unaltered preparation. The animals sensitized to the two types of diphtheria antitoxin were easily shocked with normal horse serum and also with pepsin-treated serum. Pepsin-purified serum was significantly more effective in producing shock in guinea pigs sensitized to pepsin-treated antitoxin than in those sensitized to normal horse serum. It was concluded that pepsin-treated antitoxin not only retained some of its original horse serum specificity, but also acquired a new antigenic specificity. Although there has been a reduction in the incidence of serum reactions as a result of the use of enzyme-purified antitoxin, there may eventually be an increase in reactions among persons treated with this type of serum for the second time. B. B. Siegel.

Pharmacology and Physiology

Clinical Studies With Pituitary Adrenocorticotropin. Forsham, P. H., Thorn, G. W., Prunty, F. T. G., and Hills, A. G.: J. Clin. Endocrinol. **8**: 15, 1948.

Purified anterior pituitary adrenocorticotropic hormone (ACTH) was administered to fifty subjects who had no evidence of adrenal disease and to thirty individuals with Addison's disease. Hematologic studies made with special technique showed a 74 per cent decrease in the number of circulating eosinophiles in normal individuals, while the patients with Addison's disease showed an average decrease of only 4 per cent. The response was maximal four hours after the administration of the hormone. Lymphocytes in the circulation also diminished as a result of stimulating the adrenal cortex with ACTH, but the degree of response was less than that for eosinophiles. Polymorphonuclear leucocytes increased. That the failure of patients with Addison's disease to respond to ACTH was due to insufficient adrenal cortical hormone secretion was supported by the fact that the administration of 20 mg. of crystalline 17-hydroxycorticosterone decreased their eosinophile counts by 50 per cent or more.

Initial eosinophile counts did not differ significantly between normal subjects and those having Addison's disease, suggesting that "factors other than adrenal cortical hormone regulate the basal level of circulating eosinophiles. As one of the limitations of the ACTH response it was noted that both ACTH and Compound F administered at the height of an acute allergic eosinophilia failed to reduce the level of circulating eosinophiles to the extent observed in other disorders." E. K.

Studies of the Pulmonary Circulation at Rest and During Exercise in Normal Individuals and in Patients With Chronic Pulmonary Disease. Riley, R. L., Himmelstein, A., Motley, H. L., Weiner, H. M., and Cournand, A.: Am. J. Physiol. **152**: 372, 1948.

Pulmonary artery catheterization was used to determine both cardiac output and pulmonary arterial pressure during rest and exercise. Three normal individuals and eight patients with various types of chronic pulmonary diseases including bronchiectasis and emphysema were studied. Two of the three subjects showed a fall in the mean pulmonary arterial pressure during exercise while a third showed an insignificant rise. All of the normal subjects showed a marked drop in pulmonary vascular resistance and a minimum increase in the work of the right ventricle during exercise. Three of the eight patients with chronic pulmonary disease showed an elevation of pulmonary arterial pressure at rest and all eight showed an increase in the mean pressure during exercise. Pulmonary vascular resistance during exercise in patients with chronic pulmonary disease remained stationary or was increased and the work of the right ventricle was always greater in these patients than in normal subjects at the same work level. The rise in pulmonary arterial pressure with exercise in patients with chronic heart disease is the result of decreased arterial oxyhemoglobin saturation and increased pulmonary resistance resulting from lung tissue destruction, interstitial pulmonary fibrosis, or vascular sclerosis. F.

Effect of Pulmonary Artery Ligation on the Histamine Content of Lung, With Observations on Concomitant Structural Changes. Lindskog, G. E., and Gilman, A.: Am. J. Physiol. **152**: 417, 1948.

Long-standing interruption of the pulmonary arterial flow to the right lower lobes of ten dogs produced no significant changes in the amount of extractable pulmonary tissue histamine as compared to control preoperative and postoperative determinations made on the same animals. This suggests that the high concentration of extractable histamine normally present in lung tissue is not dependent upon a filtering or clearing function exercised by the lung parenchyma on the venous blood of the pulmonary artery. These findings and the results obtained in studying lung tissue after acute and chronic injury support the hypothesis that histamine is firmly bound at some site in the lung tissue and that it is not readily released unless there is actual tissue destruction. Additional observations on lobes deprived of their pulmonary arterial blood supply showed that the weight and collapsed volume remained normal while the expanded volume diminished. F.

A Method for the Quantitative Estimation of Theophylline in Blood and Urine: Application to the Dog. Plummer, A. J.: J. Pharmacol. & Exper. Therap. **93**: 142, 1948.

Details of a method for the assay of theophylline in blood and urine are presented. There is no interference by caffeine, theobromine, uric acid, ethylenediamine, or sodium acetate. The analysis is sensitive to 0.13 mg. anhydrous theophylline per 100 ml. of blood or urine. Five dogs were injected intravenously with 8 mg. per kilogram of theophylline with ethylenediamine. Blood levels of theophylline were determined at five, thirty, sixty, and ninety minutes. The thirty-minute level was slightly more than half that found at five minutes. The sixty-minute level was less than one-third the five-minute level and theophylline could no longer be detected in the blood at the end of ninety minutes in four of the dogs. Urinalysis disclosed that 1.8 per cent of the injected theophylline appears in the urine during this period. E. K.

Comparative Effectiveness of Five Antihistaminics vs. Histamine-Induced Spasm in Canine Thiry-Vella Loops. Carver, B. N., Cameron, A., and Yonkman, F. F.: J. Pharmacol. & Exper. Therap. **93**: 168, 1948.

Over 200 experiments were carried out on dogs in which Thiry-Vella loops had been prepared. The minimal effective dose (M.E.D.) for counteracting the effects of a standard dose of histamine was determined for Antergan, Antistine, Benadryl, Neoantergan, and Pyribenzamine and was found to be constant for a given animal. When two of these drugs were combined so that one-half the respective M.E.D. of each was used or when three were combined using one-third of their respective M.E.D.'s, the response was no different from that of a single drug administered in its M.E.D. "Since the drugs proved additive in their actions, it is presumed that they act by the same or very similar mechanisms."
E. K.

An Evaluation of Antistine; A New Antihistaminic Substance. Friedlaender, A. S., and Friedlaender, S.: Ann. Allergy **6**: 23, 1948.

Antistine, 2 (N-phenyl-N-benzyl-aminomethyl) imidazolin, in doses of 10 mg. per kilogram protected guinea pigs against one lethal dose of histamine. In this respect this drug was less than 10 per cent as effective as Pyribenzamine. The clinical efficacy of Antistine was studied in 100 patients with one or more allergic complaints. The average dosage varied from 50 to 100 mg. four or more times a day. Thirty-seven per cent of twenty-four patients with bronchial asthma, 59 per cent of fifty-nine patients with vasomotor rhinitis, and seven of ten patients with acute urticaria obtained relief under this regime. Among nine patients with chronic urticaria, 33 per cent noted relief. Antistine relieved the pruritus of 60 per cent of patients with atopic eczema and 50 per cent of those with contact dermatitis. Allergic headache was relieved in only one of six patients by the drug. When the results of therapy with Antistine were compared to those of Pyribenzamine, it was found that 47 per cent of fifty-one patients with vasomotor rhinitis obtained relief from either drug; eight obtained relief with Antisteine but not with Pyribenzamine; and fourteen patients were helped only by Pyribenzamine. The effectiveness of both drugs was relatively low in asthma. Pyribenzamine was more effective in relieving the itching of allergic skin conditions. Gastrointestinal upset and drowsiness were the side reactions most commonly encountered with Antistine. Of seventy-two patients who received both drugs, 18 per cent experienced side reactions from Antistine and 38.8 per cent from Pyribenzamine. Of the patients who could not tolerate Pyribenzamine, about 64 per cent were able to take Antistine. When Antistine was used in 0.5 per cent solution on eleven patients with allergic conjunctivitis, eight experienced relief lasting several hours.
E. K. W.

The Clinical Evaluation of a New Histamine Antagonist "Decapryn." Brown, E. A., Weiss, L. R., and Maher, J. P.: Ann. Allergy **6**: 1, 1948.

The therapeutic efficacy of "Decapryn," 2[α-2 (dimethylaminoethoxy)-α methylbenzyl]-pyridine succinate, was studied in 140 allergic patients. The average dose of the drug was 12.5 to 25 mg. four times a day, although some patients received as much as 150 mg. per dose. Among fifty-four patients with asthma, 30 per cent were markedly relieved, 40 per cent were moderately relieved, and the remainder experienced no benefit. Since top dosage was given to this group, they experienced the highest incidence of side reactions. Drowsiness was reported as severe in five patients, as moderate in eleven, and as slight in sixteen patients. In forty patients with allergic coryza, twenty-nine reported excellent relief and two were not benefited. Fourteen of sixteen

patients with angioneurotic edema or urticaria were completely relieved. Among six patients with atopic dermatitis, symptomatic relief was reported as excellent in one, moderate in three, and negligible in two patients. E. H. W.

Miscellaneous

The Histaminolytic Action of Blood During Pregnancy. Anrep, G. V., Barsoum, G. S., and Ibrahim: J. Physiol. **106**: 379, 1947.

A rapid method for the estimation of the histaminolytic action of blood is described. With this method no histaminolysis was demonstrable in normal human blood, plasma, or serum, nor in bloods from patients with tuberculosis, cancer, sarcoma, "different types of allergy," advanced congestive heart failure, pleurisy, or various infectious febrile conditions. Blood taken at the time of menstruation also was devoid of histaminolytic effect. No histaminolysis was detected in the blood of dogs, cats, rats, and horses. Histamine injected into dogs and man over a period of time produced increased blood histamine levels without an increase in histaminolytic property.

In pregnant women, the blood commenced to show histaminolysis about the second month and the histaminolytic index rose to a maximum toward term. About nine hours postpartum, the histaminolytic index began to drop rapidly and was almost gone by the end of the third day postpartum. The histaminolytic principle was present in the blood serum but not in the red blood corpuscles.

The infants' sera always had much less histamine destructive power than the maternal sera. The histaminolytic action of the placenta was ten to fifteen times stronger than that of maternal serum. The amniotic fluid and extracts of umbilical cord had no histaminolytic action.

In the dog, cat, rat, mare, water buffalo, pig, and rabbit, there was no change in serum histaminolysis during pregnancy, and their respective placentae, with the exception of that of the rat, were devoid of a histaminolytic agent.

The placenta is unique in that it not only produces large amounts of histaminase but freely liberates it into the maternal blood. The function of histaminase in the blood during pregnancy is unknown. K.

Agglutination Response Following Intracutaneous Skin Testing With Brucella Abortus Antigen. Elton, N. W.: Am. J. Clin. Path. **18**: 499, 1948.

Intracutaneous tests with 0.1 ml. of a suspension of 2,000 million organisms (*B. abortus*) per milliliter Hauenstein's bacillary body suspension were made on eight healthy adults who had never had an illness resembling undulant fever. Six subjects showed definite local inflammatory reactions twenty-four hours after the injection. Agglutinins could not be detected in the sera of two of the positive reactors one week following the test. At three weeks the sera of all but two subjects contained agglutinins for *B. abortus* in titres up to 1:320. At five weeks these titres were beginning to diminish. Hence, in testing for Brucella agglutinins, blood should be drawn before the cutaneous Brucellergen test is made. E. K.

Allergy Abstracts

Asthma and Hay Fever

The Incidence and Significance of Molds in Allergic Respiratory Symptoms. Eisenstadt, W. S.: Lancet **68**: 217, 1948.

Airborne spores of fungi may be either a primary cause or a contributing factor in allergic respiratory symptoms. The dominant molds in the Minneapolis area are Alternaria, Hormodendrum, Helminthosporium, Aspergillus, Penicillium, Fusarium, Phoma, Spondyloclay, Mucor, Mycogene, and Pullularia. With the exception of Penicillium and Aspergillus, all have a seasonal incidence, being relatively sparse in the winter months and profuse in the summer months. Skin tests with mold extracts in 1:1,000 dilutions were made on a total of 380 patients ranging in age from several months to 70 years. Two hundred and forty-six were tested with eight different extracts and 124 were tested only with Hormodendrum and Alternaria. A total of 129 (34 per cent) gave positive reactions to mold extracts. Thirty-six per cent of those tested with eight molds and 33 per cent of those tested with only the two commonest offenders, Alternaria and Hormodendrum, gave positive reactions. Multiple sensitivity was the rule. Age incidence was similar to that of pollen sensitivity. Reactions proved to be clinically significant in 29 per cent of all the patients tested, and were of primary etiologic importance in 11 per cent. F.

Survey of Ragweed Pollination in the New York Metropolitan District in 1946. Walzer, E. H., Sherman, J., Chait, R. A., and Walzer, M.: New York State J. Med. **47**: 1979, 1947.

Employing the standard technique outlined by the Pollen Survey Committee of the American Academy of Allergy, a ragweed pollen survey of New York City and its metropolitan area was made. Seasonal pollen totals in all of the boroughs and in areas surrounding New York City were uniformly low. The pollen counts in Manhattan were most representative of the city as a whole. Pollen totals in Washington, D. C., Philadelphia, and Cleveland were from two to five times greater than the average total for New York City. According to the counts obtained with the old technique employed in previous years the seasonal total for 1946 in Brooklyn was only 48 per cent of the average obtained during the past eleven years. The ragweed pollen crop in New York City in 1946 was late in maturing and was relatively light. Similar conditions were also noted in neighboring states. C.

Massive Doses of Penicillin in Chronic Asthmatics. Sterling, A., Fishman, A. E., and Sharpes, F.: Am. Pract. **2**: 570, 1948.

Chronic asthmatics who had received various types of specific and nonspecific treatment were given a course of intramuscular penicillin therapy. A total of 5 million units was given to each of the patients. Three subjects developed reactions necessitating discontinuance of the treatment. Of the

twelve patients who received the full dosage, seven were apparently benefited. Improvement appeared to be the result of the specific antibiotic effect of penicillin which decreased the frequency and severity of bacterial infection. Culture studies, however, failed to reveal any significant difference before and after therapy. F.

House Dust and Fungus Allergy. Reymann, F., and Schwartz, M.: Acta Path. microbiol. Scandinav. **24**: 76, 1947.

The occurrence of sensitization to fungi found in house dust was investigated in Danish asthmatic patients. House dust specimens from twenty-two patients were used for preparation of test extracts and also for fungi cultures. The commonest fungi found in the house dust specimens were Penicillium, Aspergillus, Mucor, Alternaria, Fusarium, and Rhizopus. Six of the twenty-two patients gave positive cutaneous reactions to one or more fungi. Positive conjunctival tests could not be obtained with a 1:100 dilution of the fungi extracts. Thirteen of the twenty-two patients showed positive cutaneous reactions with autogenous house dust extracts, and five of the thirteen also had positive reactions to fungi cultured from their house dust. Of the nine patients who were negative to autogenous house dust, one showed a positive reaction to fungi present in this dust. There was no strict correlation between house dust sensitivity and fungus sensitivity. There was no evidence of the presence of a common antigen in the different fungi of the same species. It is recommended that patients be tested with extracts of fungi of the same type as those cultured from their house dust. H.

Vulvo-Vaginal Pruritus Associated with Hay Fever. Mitchell, W. F., Sivon, I., and Mitchell, J. H.: Ann. Allergy **6**: 144, 1948.

Vulvovaginal pruritus associated with ragweed pollinosis was noted in eight children ranging in age from 2 to 11 years. Hyposensitization therapy with ragweed pollen or removal to a pollen-free environment was effective in controlling this sympton. Itching was most intense in the region of the mucocutaneous junction between the vulva and vagina. The only visible skin changes were those resulting from scratching. E. W.

Pervitin Treatment of Hay Fever. Findeisen, D. J. R.: Med. Klin. **42**: 593, 1947.

Ninety-six patients with hay fever were treated for three successive seasons with "Pervitin" (methedrine-N-methyl-B-phenyl-isopropylamine hydrochloride). The average therapeutic dose required was from 9 to 12 mg. daily. Eighty-nine of the patients reported good results with the drug. Unpleasant side reactions included disturbed sleep, headache, palpitation, anorexia, and a diminished sense of well-being. No serious toxic effects were noted. H.

Dermatology

Varicelliform Eruption of Kaposi Due to Vaccinia Virus Complicating Atopic Eczema. Fries, H., Borne, S., and Barnes, H. L.: J. Pediat. **32**: 532, 1948.

The first epidemic in the United States of Kaposi's varicelliform eruption occurred in New York City in May, 1947, starting three weeks after the beginning of the mass smallpox vaccination campaign conducted in that city. Forty-three cases occurred in the city, of which sixteen came under the authors' observation. All sixteen children had atopic eczema and had never

been vaccinated. The incubation period varied from five to nineteen days. The eruption started on the eczematous areas of the face and spread to the neck, anterior thorax, and extremities. It consisted of crops of small vesicles, often umbilicated, which became larger and tended to coalesce. These went on to pustule formation followed by crusting within two days. Pruritus was intense. There was cellulitis of the face and edema of the eyes. Fever, anorexia, and restlessness accompanied the rash. The regional lymph nodes were markedly enlarged. The acute phase, the healing and convalescent periods each lasted about one week. After healing, small flat pigmented scars remained. No deaths occurred. The atopic eczema which had improved during the febrile phase later recurred.

All sixteen patients had had infantile eczema. Ten were clinically sensitive to specific foods and one had asthma. A family history of allergy was obtained in ten cases. During the acute phase of the eruption, blood eosinophilia, varying from 10 to 52 per cent, occurred in thirteen patients.

Following convalescence, vaccinations were carried out in fifteen of the sixteen patients and all showed immune reactions. Since these children had not previously been vaccinated, the immune reaction and the relationship of the outbreak of this condition to the mass vaccination program suggest the vaccinia virus as the etiologic agent. It is suggested that this condition be considered an exanthem peculiar to atopic persons with allergic eczema, the damaged eczematous skin being the portal of entry. J. SHERMAN.

Reactions to Penicillin Therapy for Syphilis. Thomas, E. W., Landy, S., and Cooper, C.: J. Invest. Dermat. **10**: 77, 1948.

In treating about 10,000 cases of syphilis with penicillin, five types of drug reactions were noted. The most common was the urticarial reaction, occurring in about 2.5 per cent of the cases treated. The incubation period was similar to that of serum sickness. In most instances, the drug could be continued in spite of the reaction. When treatment was interrupted because of severe urticaria, it could often be reinstituted after a rest period. Recurrent attacks of urticaria sometimes persisted months after cessation of therapy. Intracutaneous tests with penicillin were negative in all cases tested. The next most common reaction was an exacerbation of secondary syphilitic lesions occurring from the sixth to tenth day after the onset of penicillin therapy. Dark-field examinations of the serum from the lesions were persistently negative. These lesions lasted for from four to ten days, whether or not penicillin was continued. This type of reaction is seen only with penicillin therapy and differs from acute arsenical erythemas and delayed Herxheimer reactions. There is no adequate explanation for this phenomenon. The third type of reaction was a papular or vesiculopapular erythematous eruption appearing within the first forty-eight hours after the onset of therapy. In many of these cases there was no demonstrable fungous infection. Moreover, many cases with obvious fungous infection tolerated the drug well. A relatively unimportant type of penicillin reaction was a local reaction at the site of injection. The penicillin itself appeared to be the irritant. Two patients developed bullae on the exposed surfaces of the upper extremities. Photosensitization, as a result of penicillin, was the suspected mechanism in these cases.

No permanent sensitization to penicillin was observed and interruption of therapy because of penicillin reactions was rare. B. SIEGEL.

Iontophoresis of Pyribenzamine Hydrochloride in Pruritic Dermatoses. Aaron, T. H., Peck, S. M., and Abramson, H. A.: J. Invest. Dermat. **10**: 85, 1948.

Fifteen patients with various types of lichenified pruritic dermatoses were treated by introducing a 5 or 10 per cent Pyribenzamine hydrochloride solution into the skin lesions by iontophoresis for five minutes daily for about a week. Physiologic saline and 2 per cent procaine hydrochloride solutions were used as controls. Some relief of pruritus occurred in all patients during the course of therapy. In ten of fifteen cases, there was a complete remission at the end of the treatments, or shortly thereafter. Definite differences were noted between treated and untreated areas in cases with extensive lesions. The vesicles and lichenification disappeared, though the pigmentation remained. Iontophoresis with control solutions produced no change in the lesions. In one case, three weeks after therapy, a generalized dermatitis recurred, but the treated areas remained free. Histamine phospate in a 1:10,000 dilution, introduced into the untreated areas by iontophoresis, produced whealing and flaring, while in the treated areas, no reactions occurred. In a case of contact dermatitis due to paraphenylendiamine, positive reactions to patch tests with the contactant were inhibited by previously introducing Pyribenzamine into the sites by iontophoresis. The iontophoresis of Pyribenzamine into the abdominal skin of guinea pigs inhibited the reaction produced by applying locally varying concentrations of turpentine in sesame oil, a primary irritant. The results obtained in the above experiments are not attributed solely to the antihistaminic action of the drug, but rather to a direct inhibition of the mechanism responsible for the dermatitis. B. SIEGEL.

Allergic Eczematous Reactions of the Nail Bed. Persistent Subungual and Ungual Changes Based on Contact with "Undercoats" Containing Artificial Resins and Rubbers. Sulzberger, M. B., Rein, C. R., Fanburg, S. J., Wolf, M., Shair, H. M., and Popkin, G. L.: J. Invest. Dermat. **11**: 67, 1948.

Twelve cases of allergic eczematous reactions of the nail bed due to a nail polish undercoat, "Everon," were studied. This product is a solution of phenol formaldehyde resins and synthetic rubbers in methyl ethyl ketone. All cases showed a discoloration of almost every fingernail, a separation of the distal end of the nail from its bed, a variable amount of dark compact material under the free edge of the nail, and a variable amount of change in the visible skin of the fingertip and perionychium. The lesion usually developed rather suddenly after two to four months of almost weekly use of the undercoat. Patch tests with the finished product were positive in all cases. However, reactions varied markedly with different samples of the same undercoat and with the same sample at different times. Most cases showed positive reactions to one or more breakdown products. All cases tested with other brands of undercoats also showed positive reactions. B. SIEGEL.

Nature of Inhibition of Ultraviolet Erythema by Pyribenzamine. Preliminary Report. Kline, P. R., and Baer, R. L.: J. Invest. Dermat. **10**: 397, 1948.

Ultraviolet erythema was prevented by the iontophoresis of 5 per cent aqueous Pyribenzamine solution into the skin prior to exposure. Erythema was also inhibited by interposing the Pyribenzamine solution in a quartz cup between the skin and the source of ultraviolet radiation. Only slight diminution of ultraviolet erythema was noted when a 5 per cent solution of Benadryl was used. It is believed that Pyribenzamine exerts this inhibiting effect not by an antihistaminic action, but by absorbing those wave lengths of the ultra-

violet spectrum, 2800 to 3100 A. U., which are known to cause erythema. Benadryl is less effective because it shows no extinction at 2800 to 3100 A. U., but a moderately high extinction at 2537 angstrom units. B. SIEGEL.

The Present Status of Passive Transfer Antibodies in Allergic Eczematous Contact Type Dermatitis. Leider, M. L., and Baer, R. L.: J. Invest. Dermat. **10**: 425, 1948.

Six subjects with typical allergic eczematous contact dermatitis were patch tested for forty-eight hours with the offending allergenic agent in order to produce the dermatitis. The reactions were permitted to involute. Cantharides blisters were then raised on the healed sites. The fluids were aspirated from these blisters and immediately injected into the skin of normal subjects. Twenty-four to forty-eight hours later patch tests were applied with the specific offending allergen. The patches were removed in forty-eight hours and in all instances the tests were negative. It is concluded that it is not possible to transfer passively allergic eczematous hypersensitivity with this technique. R. WISEMAN.

Studies in Histamine (H-substance) with Special Reference to the Conditions Obtaining in Urticaria and Related Skin Changes. Nilzen, A.: Acta dermat.-venereol. **27** (Suppl.): 17, 1947.

In thirty-three normal individuals, the histamine content of the skin was 10.5 micrograms (mean value). The histamine content of the blood was 0.16 micrograms in thirty subjects. Daily variations in the blood and skin histamine were only slight. In mechanically stimulated skin, the histamine content diminished after an interval of from ten to twenty-five minutes. In dermographism, there was a reduction of the histamine content in from five to fifteen minutes. The author contends that histamine is released from the skin as a result of stimulation and is carried away. In urticaria there is a decrease in blood histamine, possibly as a result of elimination from the plasma of the histamine liberated by the corpuscles. As the urticaria diminishes, the blood histamine level increases. H.

Sensitization to Monoglyceryl Para-Aminobenzoate. Preliminary Report. Baer, R. L., and Meltzer, L.: J. Invest. Dermat. **11**: 5, 1948.

A 48-year-old man suffered two attacks of contact type dermatitis due to monoglyceryl para-aminobenzoate contained in a proprietary sunburn preventive. Strong positive reactions were obtained with patch tests with this compound. He had previously shown strong eczematous sensitization to benzocaine and a sulfonamide. Cross sensitization based on the original sensitization to the two aniline derivatives is suggested as the mechanism in this case. B. SIEGEL.

Pyribenzamine in Therapy and Prophylaxis of Rhus Dermatitis. Tweedall, D. C., and O'Conner, W. B.: J. Invest. Dermat. **10**: 301, 1948.

Twenty-eight nonselected individuals were patch tested with a 1:10 dilution of *Rhus toxicodendron* extract in acetone. The patch tests were removed after twenty-four hours and the areas cleansed. Readings were made at twenty-four-hour intervals. At the end of four days, there were five 4+ (vesiculation) reactions, no 3+ reactions, one 2+ (marked erythema) reaction, and four 1+ (mild erythema) reactions. On the sixth day, all individuals showing a 4+ reaction were retested on the opposite forearm. One hour before the test applica-

tion, 100 mg. Pyribenzamine was given orally, then 50 mg. at the time of testing, and 50 mg. every four hours for twenty-four hours. The degree of vesiculation was not influenced by the drug. Only one individual reported some relief of subjective symptoms. H.

Hyaluronidase Content of Normal and Inflamed Guinea Pig Skin. Mayer, R. L., Kochalaty, W., and Stanton, D.: Proc. Soc. Exper. Biol. & Med. **67**: 529, 1948.

Strips of normal and inflamed skin were removed from paraphenylenediamine-sensitive guinea pigs after being challenged with the antigen. Similar strips were removed from guinea pigs treated with hot water and with ultraviolet irradiation. It was found that normal guinea pig skin contained small amounts of polysaccharide depolymerizing substances, probably chiefly hyaluronidase. However, the content of hyaluronidase in allergic or heat-inflamed skin was as much as forty times as great as in normal skin. Ultraviolet-irradiated skin showed no significant increase in hyaluronidase. Negative results were obtained with skin from rabbits in which a local Arthus reaction had been produced. An explanation for the negative results may be the fact that ultraviolet irradiation and the Arthus phenomenon primarily involve the cutis, whereas the allergic and heat-induced inflammation mainly involve the epidermal tissue.
B. SIEGEL.

Otorhinology and Ophthalmology

The Significance of the Intracutaneous Test for Hypersensitivity to Uveal Pigment. McPherson, S. D., and Woods, A. C.: Am. J. Ophth. **31**: 35, 1948.

Intracutaneous tests for hypersensitivity to uveal pigment were at first read on a basis of erythema and induration at the end of thirty minutes, twenty-four and forty-eight hours. Following Friedenwald's studies, chief reliance was placed on the histologic examination of the excised skin after a two-week interval. The present study represents an attempt to evaluate the diagnostic and prognostic import of the test.

Eighty-three per cent of thirty patients with sympathetic ophthalmia gave strongly or weakly positive reactions to pigment, indicating that hypersensitivity to uveal pigment is a fairly regular concomitant of sympathetic ophthalmia. Strongly positive reactions were obtained in 14 per cent of ninety-four patients who ultimately lost their eyes as a result of injury or operation involving the uveal tract. In the remaining patients of this series, the tests gave doubtful reactions in 13 per cent and negative results in 66 per cent of cases. Of forty-five patients in whom the course after injury or operation was uneventful, none gave postive reactions, 16 per cent doubtful and 84 per cent negative reactions. It is concluded that a strongly positive pigment test after an injury or operation involving the uveal tract is a warning of a stormy postoperative course, but is not an indication that sympathetic ophthalmia will develop. Doubtfully positive and negative tests are of no prognostic significance. It is pointed out that the margin of error in both postive and negative tests is so great that their interpretation should be made only in the consideration of the clinical course. C.

Allergic Warm Season Conjunctivitis. Gutmann, M. J.: Acta med. orient. **6**: 167, 1947.

The administration of vitamins A, C, D, and K in large doses was ineffective in the treatment of allergic warm season conjunctivitis. Intramus-

cular injection of vitamin B_2 (riboflavin) in 5 mg. doses was quite effective during the acute stage of the disease, despite the fact that avitaminosis was not present. Riboflavin by mouth in no way affected the course of the disease. No explanation for the mechanism of action of riboflavin in vernal catarrh is offered. C.

Miscellaneous Allergies

Potentiating Effect of Nocardia Asteroides on Sensitization to Picryl Chloride and on Production of Isoallergic Encephalitis. Freund, J., and Lipton, M. M.: Proc. Soc. Exper. Biol. & Med. **68**: 373, 1948.

Guinea pigs were given several simultaneous deep subcutaneous injections of picryl conjugate of guinea pig stromas emulsified in paraffin oil containing killed *Nocardia asteroides* (an actinomycete, biologically close to mycobacteria). One month later, tests for sensitization were made by applying a drop of one per cent picryl chloride solution in olive oil on the skin. The majority of animals showed evidence of contact type of sensitivity. Control experiments, omitting the fungus, gave negative results. Another group of guinea pigs was injected subcutaneously with fresh guinea pig brain in water-in-oil emulsion containing killed fungi. The majority of animals developed isoallergic meningoencephalitis, the results being comparable to those obtained in experiments utilizing *Mycobacterium tuberculosis* or *Mycobacterium butyricum* as the potentiating agent. As in the latter experiments, when mice were injected with mouse or rabbit brain in water-in-oil emulsions with killed fungi, neurological symptoms of encephalitis were not observed. When the guinea pigs used in the above experiments were skin tested with an extract of *N. asteroides* at a later date, it was found that they all developed a delayed type of sensitivity to the fungus. It was also found that these sensitized animals developed a feeble sensitivity to tuberculin. B. SIEGEL.

Tuberculin Reaction. II. Cytotoxicity of Tuberculin for Splenic Explants of Desensitized Tuberculous Guinea Pigs. Kirchheimer, W. F., and Weiser, R. S.: Proc. Soc. Exper. Biol. & Med. **68**: 407, 1948.

Guinea pigs, infected with the Bacille Calmette Guérin (B.C.G.) strain of *Mycobacterium tuberculosis bovis*, that showed a necrotic reaction to an intracutaneous test with Old Tuberculin 1:100, were selected for desensitization. Gradually increasing doses of Old Tuberculin were given intraperitoneally over a period of three or four days. When the animals failed to react to Old Tuberculin 1:10, they were sacrificed. Several explants were prepared from tuberculin-sensitive and densensitized guinea pigs and incubated in tuberculin broth. Glycerine broth was employed as a control. After twenty-four hours of incubation, the mean radius of the zone of cell migration of each explant was calculated. It was found that the cytotoxic effect of tuberculin was uniformly less in the explants from desensitized animals. Results obtained with explants from tuberculin-sensitive guinea pigs, desensitized with tuberculin prepared from *Mycobacterium smegmatis*, were similar to those seen with explants of untreated sensitive animals, indicating that the desensitization with Old Tuberculin was specific. It was also found that the depression of cell migration by Old Tuberculin in splenic explants from sensitized and desensitized guinea pigs, infected with *Mycobacterium tuberculosis* H 37 Rv, was similar to that found with B.C.G. sensitized animals. These experiments are presented as further evidence for the hypothesis that the cytotoxic effect of tuberculin on tissue explants of tuberculin-sensitive animals is the result of the interaction of a sessile antibody with specific antigen. B. SIEGEL.

The Electroencephalograms of Allergic Children. Dees, S. C., and Lowenbuch, H.: Ann. Allergy **6**: 99, 1948.

Electroencephalographic studies were made on eighty-five allergic children ranging in age from 2 to 14 years. Sixty-seven of these children had had allergic disturbances for more than two years. In twenty-two patients, there was an associated convulsive disorder for which no cause could be demonstrated. The encephalograms in sixty-five of the eighty-five patients were definitely abnormal. Fifty-two of the abnormal electroencephalograms showed cerebral dysrhythmias of which forty-two were predominantly occipital and ten were frontal in type. The incidence of occipital dysrythmia was higher among the allergic group which had associated convulsive disorders than among the uncomplicated allergic group. However, the incidence of occipital dysrhythmia was signicantly greater in the latter group than in a control group of normal children. No relationship could be found between EEG patterns and the type and number of allergic complaints or the nature of the allergens. The incidence of occipital dysrhythmia increased with the duration of symptoms and with age up to 10 years. Occipital dyrshythmia occurred twice as frequently among patients with a positive family history of allergy as among those with a negative history. E. W.

Sensitivity to Streptomycin—Anaphylactic Shock with Recovery Following an Intracutaneous Test. Rosen, F. L.: J. A. M. A. **137**: 1128, 1948.

A 21-year-old nurse who had had a rash of the fingers and dorsum of the hands for a year, was skin tested with streptomycin. The patient had never received any streptomycin or penicillin therapy but had had contact with both. An intracutaneous test with 0.05 c.c. of a stock solution of streptomycin was followed in about two minutes by a severe constitutional reaction characterized by generalized pruritus, wheezing, abdominal cramps, weak, rapid pulse, and collapse. Treatment with epinephrine, Pyribenzamine and Demerol resulted in recovery. Subsequently, passive transfer studies revealed a moderate reaction to streptomycin. After forty-eight hours, the site of the direct intracutaneous test presented a typical tuberculin type of reaction. Patch tests were not done. F.

The Components of the Tubercle Bacillus Responsible for the Delayed Type of Infectious Allergy. Raffel, S.: J. Infect. Dis. **82**: 267, 1948.

Although tuberculoprotein is capable of producing anaphylactic hypersensitivity and humoral antibody response, it does not produce the delayed or tuberculin type of sensitivity. By injecting a combination of tuberculoprotein and a purified wax obtained from the tubercle bacillus, the delayed tuberculin type of hypersensitivity was regularly induced in guinea pigs. The purified wax is an ester of a polysaccharide and higher alcohols with hydroxy fatty acids. F.

Immunization of Adults with Diphtheria Toxoid. Lawrence, H. S., and Pappapenheimer, A. M.: Bull. New York Acad. Med. **3**: 334, 1948.

The proportion of undesirable reactions of a tuberculin type following the administration of diphtheria toxoid rises markedly with the age of the subjects. A group of 186 medical students and nurses were Schick tested with Schick toxin prepared by the New York City Bureau of Laboratories. Purified toxoid and P-fraction (a formalinized mixture of atoxic diphtherial proteins) diluted to Schick strength were used as controls. It was found

that both Schick positive and Schick negative individuals show allergic reactions of the delayed tuberculin type to either P-fraction or toxoid, to both, or to neither. Among the Schick positive group only three of fifty-eight individuals were highly sensitive to purified toxoid. Almost all of the Schick positive group, however, showed sensitivity to P-fraction and crude toxoid, provided they were injected in high enough dosage. Approximately 30 per cent of the Schick negative individuals showed allergic reactions to the toxoid itself diluted to Schick strength. This seems to indicate that even if toxoid were completely freed of the last traces of impurity its administration undiluted to an adult population without preliminary screening tests would result in a very high proportion of undesirable general reactions. It is concluded that purified diphtheria toxoid provides a distinct improvement over the crude toxoid in current use. However, its advantage is limited essentially to Schick positive individuals showing no sensitivity. Since a high proportion of Schick positive adults show evidence of "latent immunity" to diphtheria and produce a high titer of antitoxin in response to very small doses of toxoid, it is questionable whether immunization of older children and adults with the full dosage is necessary or advisable. C.

Anaphylaxis

Anaphylaxis XVIII: Studies on Passive Sensitization of the Dog. Sherwood, N. P., Stoland, O. O., Kirk, J. S., and Tennenberg, D. J.: J. Immunol. **59**: 279, 1948.

Thirty-four dogs were each passively sensitized with 10 ml. of homologous antihorse serum per kilogram of body weight. The latent period between injection of the immune serum and the antigen varied from zero to seventy-two hours. In a group of fourteen dogs in which the latent period was eliminated and the antigen and antibody were injected simultaneously all showed typical anaphylactic shock immediately. In a group of four dogs in which the latent period varied from one to six hours, shock developed immediately following the intravenous injection of the antigen. When the latent period was from twenty-two to seventy-two hours, only three of sixteen animals could be shocked. It appeared that a latent period was unnecessary in passive sensitization of the dog with homologous immune serum. Apparently there is great variation in the ability of dogs either to excrete or to destroy antibodies. Because of the absence of a latent period in passive sensitization of dogs, the minimum sensitizing dose of any immune homologous serum can readily be determined by the use of constant dosages of antigen. R. WISEMAN.

Prevention by Sodium Salicylate of Arteritis in the Experimental Allergic State. Sullivan, C. J., Parker, T. W., and Hibbert, R. W.: Proc. Soc. Exper. Biol. & Med. **67**: 508, 1948.

Four groups of rabbits were actively sensitized by intravenous injections of horse serum. Precipitin titers against horse serum were checked on several occasions during the period of sensitization. One week after the last injection, the animals were sacrified and the organs examined for the presence of arteritis. One group of rabbits had been treated with para-aminobenzoic acid daily for a month prior to the first injection of horse serum and during the sensitization period. The second group had received daily subcutaneous injections of sodium salicylate starting eight days prior to the onset of sensitization until the animals were sacrified. The treatment of the third group was similar to the second, except that an intravenous injection of sodium salicylate was given prior to the first injection of horse serum. The last

group served as a control, receiving horse serum alone. It was found that the animals treated by subcutaneous injections of sodium salicylate showed no evidence of arteritis and moderate or slight quantities of circulating antibody. Those animals treated with intravenous sodium salicylate first showed definite evidence of arteritis and very low precipitin titers. Animals treated with para-aminobenzoic acid and control animals showed high antibody titers and arterial lesions. It is believed that the sodium salicylate given subcutaneously prevented arterial lesions, in spite of the presence of moderate amounts of circulating antibody by interfering with the union of antigen and tissue cells. B. SIEGEL.

Release of Proteolytic Enzyme in Anaphylactic and Peptone Shock in Vitro. Ungar, G.: Lancet **252**: 708, 1947.

Previous studies have indicated that the release of histamine is connected with proteolysis. Protease and antiprotease were titrated by a technique based on the inhibition of clotting of fibrinogen by protease. When the specific antigen (egg white) was added to minced lung, liver, and kidney tissue of sensitized guinea pigs, protease was liberated within fifteen minutes. Peptone mixed with normal guinea pig tissue and serum also brought about the release of protease. The anti-protease titer dropped in sensitized guinea pig serum or normal serum following mixture with antigen or peptone respectively. There was no significant difference in antiprotease levels in the sera of sensitized and normal animals. No enzyme was released from normal guinea pig tissues by the antigen. Protease was liberated from normal tissues by peptone and from sensitized tissues by homologous antigen regardless of the potentiality of these tissues to release histamine. There was a more marked response to peptone than to antigen in vitro whereas peptone in vivo caused only relatively mild shock. The explanation of this is unknown. K.

The Precipitation of Latent Herpes Simplex Encephalitis by Anaphylactic Shock. Good, R. A., and Campbell, B.: Proc. Soc. Exper. Biol. & Med. **68**: 82, 1948.

Young adult albino rabbits, actively sensitized to egg white, were injected intramuscularly with suspensions of herpes simplex infected mouse brain. About 50 per cent of the animals died within three to four weeks from acute encephalomyelitis. The remaining animals either recovered from the acute phase, ran a chronic course, or gave no demonstrable evidence of infection. Rabbits which remained asymptomatic for from one to three months were then shocked with an intravenous injection of egg white. Of forty-four animals suspected of having a latent herpes simplex infection, sixteen developed encephalomyelitis after they were shocked. The incubation period from the time of shock and the exacerbation varied from two to fourteen days. There was little correlation between the severity of shock and the incidence of activation of the latent infection. Herpes simplex virus was recovered from the central nervous system following fatal anaphylactically precipitated encephalitis. It is suggested that there is a renewal of the disease process when rabbits with latent herpetic infection are shocked. This precipitation may occur as a result of a temporary lapse of the immunity to the virus during anaphylactic shock. B. SIEGEL.

Pharmacology and Physiology

Effect of Benadryl Hydrochloride on the Tuberculin Reaction in Guinea Pigs. Sarber, R. W.: Am. Rev. Tuberc. **57**: 504, 1948.

Guinea pigs infected with a mixture of human and bovine strains of *Mycobacterium tuberculosis* were tested with serial dilutions of tuberculin before and after the administration of Benadryl. Benadryl was administered subcutaneously, twice daily. Forty-eight hours after the initial dose, twenty-two infected guinea pigs and three controls were retested with tuberculin (P. P. D.). Benadryl was continued until the forty-eight-hour readings were made. Benadryl decreased the size of the reactions and markedly reduced the incidence of necrosis. Repetition of the study using Old Tuberculin yielded similar results. The dose-response curve in animals treated with Benadryl parallels, at a lower level, that of untreated animals. It is suggested that previous reports of failure to observe this effect of Benadryl on the tuberculin response were due to inadequate and insufficiently sustained dosage and failure to employ threshold doses of tuberculin. K.

Evidence for an Adrenergic Component in the Nervous Mechanism of Sweating in Man. Haimovici, H.: Proc. Soc. Exper. Med. & Biol. **68**: 40, 1948.

The effect of Dibenamine, administered intravenously to twenty-four subjects with hypertension or other vascular or neurological conditions, was studied. Sweat prints, obtained by applying tannic acid treated paper to skin painted with ferric chloride, and thermometric changes were recorded before and after the administration of Dibenamine. It was found that the adrenergic blocking drug either produced total or partial suppression of sweating. Intravenously injected Neosynephrine induced moderate sweating, but was without effect when given after Dibenamine. However, sweating induced by mecholyl was not influenced by a previous administration of Dibenamine. It is thus concluded that in addition to the known cholinergic fibers supplying the sweat glands, there is also an adrenergic component in the nervous mechanism of sweating in man. B. SIEGEL.

Miscellaneous

Antiproteins in Horse Sera. IV. Antibodies to Rabbit Serum Globulin and Their Interaction with Antigen. Treffers, H. P., Heidelberger, M., and Freund, J.: J. Exper. Med. **86**: 95, 1947.

Horses injected intravenously with alum-precipitated rabbit serum globulin produced precipitin-type antibodies characterized in vitro by the absence of a prezone in the region of antibody excess. The serological, chemical, electrophoretic, and other physical properties of these antibodies were similar to those of pneumococcus anticarbohydrate (precipitins). When the intracutaneous or subcutaneous route of sensitization was subsequently used in the same horses, there appeared a "univalent" antibody which did not precipitate with soluble antigen but could be removed from solution by coprecipitation in the presence of multivalent precipitating antibody or by attachment to preformed specific precipitates. The precipitating antibody did not reappear in these horses when the route of injection was changed from the intravenous to the subcutaneous or intracutaneous, suggesting an essential independence of these physiological mechanisms for producing the two forms

of antibody. In summary, "the antibody formed in response to subcutaneous injection of globulin differs most strikingly from that produced after intravenous injection in its failure to precipitate with globulin in solution." K.

The Diffuse Collagen Diseases. A Morphological Correlation. Duff, G. L.: Canad. M. A. J. **58**: 317, 1948.

The concept of disease entities affecting a specific kind of tissue, such as connective tissue, serves to integrate the widespread and varied lesions appearing in each of such diseases as rheumatic fever, lupus erythematosus, periarteritis nodosa, diffuse scleroderma, dermatomyositis, rheumatoid arthritis, serum sickness, Buerger's disease, and lesions induced by the injection of foreign protein in experimental animals. The characteristics of connective tissue and the pathologic sequences in several of the above-mentioned diseases are described in detail. Fibrinoid necrosis is frequently observed in lesions associated with tissue hypersensitivity but may also occur in diseases not commonly associated with allergy, such as the necrosis in the base of a peptic ulcer or in the renal arterioles of malignant hypertension. It is postulated that a variety of factors, of which hypersensitivity is one, may lead to the release of enzymes in connective tissue followed by destruction of collagenous and elastic fibers and changes in the intracellular ground substance. Morphological similarities in the lesions of the "collagen diseases" do not necessarily imply an initial common etiology. K.

Psychromatic Aspects of Allergic Disorders. Weiss, E.: Bull. New York Acad. Med. **5**: 604, 1947.

The allergic and the neurotic populations are numerous so that these disorders exist together in many people. Personality studies suggest a more intimate connection, a specific relationship between neurotic character structure and allergic disorder, representing parallel manifestations of the same basic fault, the one discharging on the level of psychic representation through thoughts and feelings and the other on the physiological level by means of disturbances in organ functioning. Thus, in allergic disorders such as asthma, migraine, and neurodermatitis, physical and psychological factors act in a complementary fashion to produce the disorder; in one instance, specific physical factors may predominate, in another, specific emotional factors.

The allergic disorders fall into the group of organ neuroses that can be termed vegetative, representing early and profound deviations of personality development. Proper management depends on the evaluation of physical and psychological factors. Psychotherapy plus the allergic approach will mean better treatment for the individual with an allergic disorder. C.

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